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The Burden of Hypoglycemia during Real-World Conditions

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Background:
Although management of type 1 diabetes (T1D) has improved with the introduction of novel insulins and modern technology, hypoglycemia is still a common problem. Little is known about real-world data on hypoglycemia in people with T1D using the flash glucose monitoring (FGM). The aim of the present analysis is to assess the occurrence of hypoglycemia in a registry of T1D over the course of a year.

Method:
We analyzed registry data collected at a tertiary diabetes center. Adult patients with T1D routinely using FGM and with sensor coverage >80% of time were eligible for analysis. Episodes of hypoglycemia (<3.9mmol/L and <3.0mmol/L) and duration of hypoglycemia detected by FGM were determined. Hypoglycemic episodes were defined as follows: beginning of the FGM event – readings below the threshold for at least 15 min; end of the FGM event - readings for 15 min >3.9 mmol/L; prolonged hypoglycemic event - FGM levels are <3.0 mmol/L for consecutive 120 min or more. Additionally, time below range <3.9 mmol/L (TBR), time in range 3.9-10.0 mmol/L (TIR) and time above range >10.0 mmol/L (TAR) were analyzed for the population.

Result:
N=44 patients (36.7% female, mean age: 39.7 ± 14.4 years, diabetes duration 15.5 ± 12.4 years, 100% Caucasian, BMI 24.4 ± 3.6 kg/m², A1c 59 ± 11 mmol/mol, insulin pump vs. injection therapy: 13.6%. vs. 77.3%, 9.1% used both delivery methods during the observational period) were included in the analysis. Mean observation period was 13.7 ± 4.6 months. Mean number of hypoglycemic episodes <3.9mmol/L and <3.0mmol/L during the observation period was 221.7 ± 143.4 and 93.5 ± 99.1, respectively. Mean duration per hypoglycemic episodes <3.9mmol/L and <3.0mmol/L was 50.8 ± 32.2 and 76.2 ± 63.8 minutes, respectively. TAR, TIR and TBR were 40.3 ± 19.1%, 53.9 ± 17.5% and 5.1 ± 4.3%, respectively.

Conclusion:
In a T1D population routinely using FGM, hypoglycemia is still frequent and the average duration of an episode is long.

Creating Virtual Simulation Scenarios that Mimic Clinical Data Acquired from Patients with Type 1 Diabetes

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Objective:
The objective of this research work is to replicate real-life scenarios encountered by patients with type 1 diabetes (T1D) and high glycemic variability to challenge newly-developed controllers.

Method:
The real-life meal scenario, basal insulin, and bolus insulin were extracted from Medtronic 670G insulin pump (Northridge, CA, USA) data for a cohort of N=14 patients with T1D from the Hospital Clínic de Barcelona and incorporated into the simulator. Next, using a detection algorithm, disturbances from the clinical data were added to the scenario in the form of aerobic exercise. A duration of 14 days was used for generating the scenario using the UVA/Padova simulator. The insulin sensitivity and the variability in insulin sensitivity were adjusted day-by-day to achieve a blood glucose profile and a coefficient of variation (CV) for the clinical data, respectively.

Result:
The simulator results obtained replicated clinical data outcomes with an error of less than 10%. The main parameters considered were median value of glucose concentration and CV. The median value of glucose reflects the glucose profile of the patients and the CV indicates the variability in glucose values. Good approximations of time-in-range were also achieved.

Conclusion:
The methodology used in this work appears to be capable of creating realistic scenarios that mimic real life behavior in order to produce data similar to clinical outcomes for a specific population of patients with T1D. This enables controllers aimed at optimizing blood glucose in T1D patients to be tested using difficult real-life scenarios thus, ensuring its success in real-life applications.

In-silico Insulin Estimation Using an Extended Kalman Filter

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Objective:
The availability of insulin concentration measurements from an immunosensor may enhance glucose control and the automation of automated insulin dosing (AID) systems. The aim of this work is to assess the ability of an Extended Kalman Filter to estimate the postprandial excursions of capillary insulin concentration from baseline levels at mealtime with different measurement intervals.

Method:
We propose a nonlinear discrete-time observer based on an insulin pharmacokinetic model augmented with a capillary compartment, for which the plasma insulin elimination rate follows Michaelis–Menten kinetics. In order to evaluate the observer performance, the estimated excursions from baseline were compared to the excursions obtained by a microneedle insulin immunosensor and laboratory-based ELISA insulin measurements of four adults with type 1 diabetes (T1D) (mean age: 43±12 years). Using the UVA/Padova Simulator, we evaluated the observer across ten subjects with measurement samples occurring at 5-, 30-, 60-, 120-, and 180-minute intervals, using the immunosensor noise standard deviation of 20.64 pmol/L.

Result:
The prediction errors of the observer were determined by assessing the concordance between the estimated and the measured insulin differences, which were obtained by comparing the postprandial insulin measurements to the mealtime measurement. The median root-mean-square errors between the estimated delta insulin values and the immunosensor and ELISA delta changes were 22.47, 10.90, 9.65, 9.87, 10.64, 12.01 pmol/L and 22.11, 14.52, 14.18, 14.20, 15.18, 16.35 pmol/L for each measurement interval, respectively.

Conclusion:
We present a nonlinear observer to track the excursion of insulin concentration levels measured by the immunosensor and the laboratory-based ELISA. Future work will focus on using the observer to study the integration of an insulin immunosensor to enhance the design of an augmented closed-loop.

Exploration of the Availability and Features of Diabetes Self-management Applications on the App Stores

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Objective:
This study aims to explore the availability and features of mobile applications in Google Play Store® (Android™), for the self-management of type 1 and type 2 diabetes in adults in English and Arabic languages. It also aims to compare these features with AADE7 Self-Care Behaviors®.

Method:
A web-based search performed through the Google Play Store® (Android™). The search was conducted in July 2020 to identify applications that are specifically designed for the self-management of diabetes in the English and Arabic languages for type 1 and type 2 diabetes. Each application that meets the inclusion criteria has been downloaded, and its features explored and compared to recommended AADE7 Self-Care Behaviors®.

Result:
There were N=402 application results from the search. Of those, N=45 apps met the inclusion criteria and N=357 did not and were excluded. Included applications, N=43 apps in English and N=2 in Arabic and support a range of Self-Care Behaviors: 53% Healthy Eating, 42% Being Active, 96% Monitoring, 49% Taking Medication, 11% Problem Solving, 20% Reducing Risks, and 53% Healthy Coping. Only one application supports all areas of Self-Care Behaviors.

Conclusion:
The available applications are limited to supporting only some self-management tasks. Patients are required to install different tools for the self-management of their diabetes but not all tools are available to perform all of the self-diabetes management tasks. Future development should aim to develop a comprehensive evidence-based application to support all areas of Self-Care Behaviors.

The Impact of a Prolonged Lockdown and Use of Telemedicine on Glycemic Control in People with Type 1 Diabetes During the COVID-19 Outbreak in Saudi Arabia

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Objective:
To minimize the spread of COVID-19, Saudi Arabia imposed a nationwide lockdown for over 6 weeks. We examined the impact of lockdown on glycemic control in individuals with type 1 diabetes (T1D), using continuous glucose monitoring (CGM); and assessed whether changes in glycemic control differ between those who attended a telemedicine visit during lockdown and those who did not.

Method:
Flash CGM data from n=101 individuals with T1D were retrospectively evaluated. Participants were categorized into two groups: Attended a telemedicine visit during lockdown (n=61) or did not attend (n=40). Changes in CGM metrics over 6 weeks of lockdown, from the last 2 weeks pre-lockdown to the last 2 weeks of the complete lockdown period, were examined in the two groups.

Result:
Among individuals with T1D, with the following characteristics [Medians (IQR) age: 23 (18,28) years old; diabetes duration: 7 (3,16) years; females: 54.46%; and insulin pump users: 28.57%], those who attended a telemedicine visit during lockdown had an improvement in the following CGM metrics by the end of lockdown: Average glucose (from 180 to 159mg/dl, $p<0.01$), glycemic management indicator (from 7.7 to 7.2%, $p=0.03$), time in range (from 46 to 55%, $p<0.01$), and time above range (from 48 to 35%, $p<0.01$) without significant changes in time below range, coefficient of variability, or number of daily scans or hypoglycemic events. In contrast, there were no significant changes in any of the CGM metrics during the lockdown period in those who did not attend any telemedicine visit.

Conclusion:
A six-week lockdown did not worsen, nor improve, glycemic control in individuals with T1D who did not attend a telemedicine visit. Whereas those who attended a telemedicine visit had a significant improvement in glycemic metrics; supporting the clinical effectiveness of telemedicine in diabetes care.

Predictors of Use and Improvement in Glycemic Indices After Initiating Continuous Glucose Monitoring in Real World: Data from Saudi Arabia

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Objective:
To identify predictors of use and benefit from continuous glucose monitoring (CGM) in people with type 1 diabetes (T1D).

Method:
Changes in glycemic indices, weight, lipid parameter, and albumin:creatinine ratio (ACR) after using intermittently-scanned CGMs for one year were examined in 116 individuals. Participants were categorized based on frequency of sensor scanning at month 6 into: Frequent scanners (≥10 CGM scans/day) and infrequent scanners (<10 scans/day). Adjusted regression models examined the association of potential predictors with improvement to time in range (TIR), time below range (TBR), and frequency of sensor scanning at month 6.

Result:
Average sensor glucose, TIR, TBR, time above range (TAR), and glycemic management index (GMI) have all improved significantly from baseline to month twelve (176.5 to 164 mg/dl, 43 to 50.5%, 7 to 5.5%, 48.5 to 39%, 7.8 to 7.3%; respectively, all $p<0.05$) without significant changes in average scans/day, weight, lipid, or ACR (all $p>0.05$). Frequent scanners had an improvement in TIR and TAR at both month 6 and 12; whereas infrequent scanners only had a comparable improvement at month 12. Individuals with baseline TIR<50% had a significant improvement in TIR and TAR; whereas those with baseline TIR ≥50% had an improvement in TBR only. Baseline TIR <50% and frequency of scans were predictive of improvement in TIR at month 6 (OR: 4.84, $p<0.01$ and 1.05, $p=0.04$; respectively); whereas baseline TBR was the only predictor of improvement in TBR (OR:1.24, $p<0.01$). Being a woman, higher number of scans/day in the first 2 weeks, and having lower A1C at baseline were predictive of being a frequent scanner at month 6 (OR: 2.81, $p=0.04$; 1.12, $p<0.01$; and 0.73, $p<0.01$; respectively).

Conclusion:
Use of CGM improves glycemic control in individuals with T1D; and success can be predicted by frequency of sensor scanning at 6 months and baseline TIR.

Deteriorating Glucose Control in Patients with Diabetes (PWD) after Disengagement from A Mobile Health (mHealth) App

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Objective:
Connected diabetes devices and mobile apps can be valuable for diabetes self-management, but the usage of such tools can be inconsistent in the real world. Discontinued use of self-management tools can lead to deteriorating outcomes and increases the risk of complications. In the current study, we investigated the glycemic and behavioral outcomes of patients with diabetes (PWD) users of a mHealth self-management app prior to and following disengagement to better understand how discontinued use of the app (i.e., dropout) may affect PWDs' diabetes management.

Method:
We randomly selected N=472 PWD users of a diabetes management app who uploaded their diabetes device (glucose meters and/or insulin pumps) data remotely and at clinic appointments. To compare glucose outcomes prior to and post dropout, we selected PWDs who discontinued remote in-app device uploads after a minimum of 6 weeks of consistent use, but who subsequently uploaded their diabetes devices at a clinic visit after dropping out.
We compared diabetes outcomes (i.e., average blood glucose (BG), percent of readings in range, percent of readings in hyperglycemia range, percent readings in hypoglycemia range, and number of daily glucose checks) before and after dropping out using paired t-tests.

Result:
The cohort had median age=19 years (IQR 13-47), 53% female, and 70% self-reported as having type 1 diabetes. The average BG increased from 188mg/dL during the 2 weeks prior to dropping out to 193mg/dL at 6-8 weeks after dropout($p=0.004$). The percent of readings in range (70-180mg/dL) decreased from 46.3% to 44.6%($p=0.03$). The percent of readings in hyperglycemia (>180mg/dL) increased from 45% to 48%($p=0.02$). The average number of glucose checks decreased from 4 to 3.7 daily checks over the same time period ($p<0.00001$). We did not observe any changes in percent hypoglycemia.

Conclusion:
The present analysis indicates that disengagement with a mHealth app is predictive of worsening glucose control. Dropout risk is inherent to novel diabetes management technologies. Whether the risk of disengaging with novel technologies can be mitigated via remote patient monitoring and advanced predictive analytics remains to be determined.

Closed-Loop Insulin Delivery in Adults with Highly Unstable Type 1 Diabetes can Outperform Suspend-before-Low Insulin Pump Technology: A Feasibility, 16-week Randomized Crossover Trial

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Objective:
Our objective was to assess whether the Diabeloop DBLHU hybrid monohormonal closed-loop system could improve glucose control in patients with highly unstable diabetes, compared to a predictive low glucose suspend system (PLGS).

Method:
In this controlled, randomized, feasibility trial, we recruited adults with type 1 diabetes with severe glucose instability experiencing severe hypoglycemia with a theoretical indication for islet transplantation. After a 2-week run-in period, patients went through a series of N-of-1 trials including two blocks of two periods of four weeks each. Within each block, the sequence DBLHU/PLGS or PLGS/DBLHU was randomized. The primary outcome was the percentage of time spent in the 70 – 180 mg/dL glucose range measured on the third and fourth week of each sequence. Statistical analysis was performed on the complete set. This trial is registered with ClinicalTrials.gov, number NCT04042207.

Result:
N=7 patients were randomized and N=5 completed the trial as planned. Using DBLHU was associated with a 29·8% higher (95% CI 25·1 to 34·6, p<0·0001) percentage of time in the 70 – 180 mg/dL glucose range (73·3% (1·7) vs. 43·5% (1·7)), and improved secondary outcomes: glucose variability, satisfaction score, and perceived frequency of hypoglycemia. There were no treatment-related adverse events during the study..

Conclusion:
The DBLHU system may be an effective option for the unmet medical need of unstable type 1 diabetes. Closed-loop should be considered ahead of islet transplantation.

Using Dielectric Spectroscopy in Diabetes: Performance of the Alertgy Non-invasive Continuous Glucose Monitor (ANICGM)

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Introduction:
The Alertgy non-invasive continuous glucose monitor (ANICGM) is a novel device that does not entail skin puncture. This study evaluated the performance of the ANICGM compared with an FDA-approved glucose meter in patients with type 2 diabetes.

Method:
The ANICGM device measures changes in the electromagnetic field generated by its sensor to produce a dielectric spectrum. The data contained within this spectrum are used in tandem with machine learning algorithms to estimate BG. Values from the ANICGM were compared to BG using the Accuchek Inform II glucometer. Fifteen patients completed three 120-minute sessions. Two different algorithms were used for BG prediction. Algorithm A estimates were generated using a model developed with data from a prior study in addition to data from this study. Algorithm B estimates were produced using a model that incorporated only the present study cohort. Mean absolute relative difference (MARD) was calculated for each study day using both algorithms.

Result:
Across all study days, percent mean absolute relative difference (MARD%) was lower using Algorithm B compared to Algorithm A. For Days 2&3, MARD decreased from 34.9% to 16.5% ($p<0.001$). For both algorithms, MARD for Days 2&3 was higher than Day 1. For Algorithm A, Day 1 MARD was 29.4% and Days 2 & 3 MARD was 34.9% ($p=0.31$). In Algorithm B, MARD increased from 7.6% on Day 1 to 16.5% for Days 2 & 3 ($p<0.001$).

Conclusion:
These data show a strong correlation between ANICGM and FS BG measurements. This technology shows promising advances towards development of a noninvasive CGM.

Simulating Subcutaneous Tissue Using Ballistic Gel and Polyurethane Film for Infusion Set Insertion Force Testing

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Objective:
Establish a tissue simulator made of ballistic gel and polyurethane (PU) rubber film as a suitable model for measuring infusion set insertion force into subcutaneous tissue.

Method:
Three grades of ballistic gel, Gelatins #0, #1, and #2, were assembled with a 0.015" PU rubber film surface layer. Gelatins #0 through #2 have a Young's Moduli of 726 kPa, 668 kPa, and 485 kPa, respectively which simulates subcutaneous tissue. A 0.015" thickness PU film was added to simulate dermis. Each assembly was pierced 10 times with a new 27G hypodermic needle and a compression testing machine operating at 140mm/min. This process was repeated using pig abdomen (freshly harvested, unscalded skin) for an additional 20 insertions. The maximum resistance force measured per insertion was recorded and analyzed. Comparison between tissue simulator and pig tissue was made using a two-tailed t-test and a p-value of 0.05 for statistical significance.

Result:
The average maximum insertion force (and standard deviation) for Gelatin #0, #1, and #2 assemblies was 0.71 N (0.04), 0.68 N (0.08), and 0.69 N (0.05), respectively. Pig abdomen required an average maximum insertion force of 0.48 N with a standard deviation of 0.11 N. A two tailed t-test was performed between the pig abdomen and Gelatin #0 and resulted in p-value of <0.001, demonstrating a statistically significant difference between the two populations.

Conclusion:
Gelatin #0 with a 0.015" PU film surface layer provided an insertion force that was less variable than Gelatins #1 and #2, but greater than that required to pierce pig abdomen tissue. This assembly was selected as a reasonable tissue simulator challenge medium for use in infusion set insertion verification testing.

Determining the Optimal Duration of a Clinical Trial Having Time-in-Ranges as Final Endpoints

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Objective:
Determining the optimal duration of CGM recordings to accurately assess time in different glucose ranges (TIRs) is crucial for the design of clinical trials evaluating overall glycemic control. Too short monitoring periods provide a poor estimation of TIRs, affected by weekly fluctuations, while extremely long trials result in excessive costs not justified by real benefits. In this work, we propose a mathematical approach to determine the minimum CGM duration warranting a desired level of accuracy for TIRs estimate.

Method:
Framing the problem as a random variable estimation problem, we derived a mathematical formula linking the number N of monitoring days with the uncertainty of TIRs estimate, expressed as standard deviation SD (Camerlingo et al., Sci. Rep., 2020). The formula was tested on CGM data of N=148 subjects with type 1 diabetes and was effective for predicting the uncertainty of time in range: 70-180 mg/dL (TIR), time below range: <70 mg/dL (TBR), and time above range: >180 mg/dL (TAR).

Result:
For a CGM system with 5-min sampling rate, N=30 days provide a SD of 6.31% for TIR, 12.1% for TAR, 27.2% for TBR, meaning that an estimated 60%, 35%, and 5% of TIR, TAR, and TBR, respectively, are associated with ±3.78%, ±4.24%, and ±1.36% confidence intervals. Furthermore, the formula suggests 56 days to reduce the SD of TBR at 20% and 48 days to reach a SD of 5% for TIR.

Conclusion:
We derived and validated a mathematical formula to estimate the uncertainty of TIRs already estimated from past clinical trials. This formula can also be used proactively to select the minimum CGM duration granting a desired level of accuracy, which is particularly significant in terms of clinical relevance and cost-effectiveness.

ReplayBG: A Novel *In-Silico* Framework to Retrospectively Assess New Therapy Guidelines for Type 1 Diabetes Management

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Objective:
Design and assessment of new therapy guidelines for type 1 diabetes (T1D) management can be greatly facilitated by retrospective data analysis and simulation, in particular by comparing the actually measured CGM trace with the glucose time-course that "would have been obtained" by adopting, in the same subject, the new therapy guideline under test. Predicting this time-course by straightforward modeling methodologies can require strong hypotheses that unavoidably narrow the domain of validity of the inferred results (Vettoretti et al. Diabetes Technol Ther, 2016). The ReplayBG framework proposed in this work avoids this limitation.

Method:
First, a non-linear model of glucose-insulin dynamics is determined, using a Bayesian strategy, on retrospective patient data where the inputs are insulin infusions and carbohydrate intake and the output is CGM. The so-identified model is then used to simulate and compare i) the CGM trace obtained by "replaying" the recorded scenario and ii) the CGM trace obtained using the insulin/carbohydrate input proposed by the therapy treatment under evaluation. To demonstrate the use of ReplayBG, we retrospectively compared, in fourteen T1D patients monitored for five months, a recently developed insulin dosing strategy (Noaro et al., IEEE Trans Biomed Eng, 2020) against the standard formula for bolus computation.

Result:
Results show that, with a limited computational time, ReplayBG is able to reliably assess new therapy guidelines for T1D. The considered demonstration suggests that the insulin dosing strategy of Noaro et al. outperforms the standard formula in terms of glucose control indices.

Conclusion:
ReplayBG does not rely on possibly critical assumptions made by other methods proposed in the literature and can safely be used to preliminarily evaluate new therapies for T1D management before moving to clinical trials.

Fluid Path Stability and Infusion Set Occlusions Comparison

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Objective:
Preliminary findings from the development of *in-vitro* and *in-vivo* insulin infusion set (IIS) test models indicate that inflammatory response, macrophage number, and device wear-time were significantly impacted by preservative loss and levels of aggregates or particles. This study compared the impact of changes in insulin preservative, impurities and aggregates, in Medtronic and non-Medtronic insulin infusion pumps, during evaluation of fluid path stability and IIS occlusion.

Method:
Fast-acting insulins (Novolog® and Humalog®) and a faster-acting insulin (Fiasp®) were pumped under simulated-use conditions through Quick™-set infusion sets with Paradigm™ pumps (and shaken reservoirs) or Autosoft™ 90 infusion sets with non-Medtronic pumps (and shaken cartridges). The *in-vitro* insulin studies were conducted for twice the labeled IIS wear-time. Insulin stability in *in-vitro* pumped insulins and non-pumped insulin controls were analyzed.

Result:
The *in-vitro* Humalog®-pumped data showed that impurity gains and preservative losses in samples from the non-Medtronic pump and cartridges were greater compared to those observed in Paradigm™pump and reservoir samples, respectively. The *in-vitro* Novolog®- and Fiasp®-pumped data showed a substantially higher concentration of aggregates in non-Medtronic pumped samples and caused fluid path occlusion.

Conclusion:
These data help support previous test model findings and indicate that a fluid path system (i.e., reservoir or cartridge, IIS and the interface connection) design that reduces preservative loss and propagation of aggregates may improve IIS wear-time and potentially optimize closed-loop insulin delivery therapy.

Insulin Cost-Savings Comparison: 7-Day Extended Wear Infusion Set with a Medtronic Pump vs. 2-3 Day Wear Infusion Set with a Non-Medtronic Pump

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Objective:
Most soft-cannula insulin infusion sets are labeled for either 2 days or 3 days of infusion. The potential insulin savings associated with extending the duration of infusion set wear from 2-3 days to 7 days has been recently determined. This study compared insulin waste reduction and its cost savings (based on U.S. insulin pricing) in both Medtronic and non-Medtronic insulin infusion pump systems under labeled infusion set wear durations (i.e. 2 days, 3 days and 7 days).

Method:
The discarded insulin volume in the reservoir, cartridge, insulin transfer syringe and infusion set under a current-wear scenario of 2 to 3 days versus 7 days with different insulin pump delivery systems was modeled and tested. A mix of use-cases for an infusion set/reservoir (or cartridge) with different insulin pump delivery systems (Medtronic and non-Medtronic) was used to compute the insulin cost savings (~$450/insulin vial).

Result:
In comparison to non-Medtronic insulin pump users, the average annual reduction in discarded insulin volume for Medtronic pump users was calculated to be about 7-9 vials of insulin per year for a 7-day infusion. The corresponding cost reductions per pump user as a result of insulin savings was ~$3,150 to $4,050 per year.

Conclusion:
These data suggest that using insulin infusion sets that last for 7 days, with a Medtronic insulin infusion pump system, can yield substantial cost savings to patients, private health plans, and other payers (e.g., Centers for Medicare and Medicaid Services).

Characterizing the Effect of Physical Activity for Blood Glucose Management in People with Type 1 Diabetes (T1D)

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Objective:
To investigate the relationships between physical activity and glucose dynamics with linear mixed effect models (LMEMs) in patients with T1D in various conditions.

Method:
Data collected during the DIAdvisor™ project from N=50 T1DM subjects (33M/17F, age 40±12 [yr], disease duration 19.4±10 [yr], BMI 24.8±2.8 [kg/m^2], A1c 7.8±0.9 [%], 28 MDI and 22 CSII) during 2 visits (75-hour in-hospital and 7-day ambulatory setting) included: interstitial glucose measurements (BGM) [1Hz] sampled with Abbott Freestyle™, accelerometer data [1Hz] recorded with ViVoMetrics Clinical LifeShirt™ and patients annotated meal intake and insulin injections. For each period from 90 minutes before to 180 minutes after a meal, LMEMs were used to assess physical activity as the magnitude of the accelerometer 3D-jerk [m/s^3]. Fixed effects were estimated from the glucose dynamics: BGM value [mg/dL] and timing [min] of base and peak, time difference [min] between base and peak BGM; BGM rate of increase post-meal [mg/dL-min]; insulin bolus [u], carbohydrate [g] and area-under-the curve [min-mg/dL].

Result:
Median values for (in-hospital, ambulatory) visits were: *jerk* (1.58, 1.93) [m/s^3], *bgm_base* (108.5, 102.5) [mg/dL], *bgm_rate_increase* (0.75, 0.57) [mg/dL-min], *carbohydrate* (43,40) [g], *insulin_bolus* (45.3, 47.55) [u], *bgm_peak* (171.5, 169) [mg/dL], *t_bgbase_to_bgpeak* (70, 70) [min], *AUC*(3510, 3695) [min-mg/dL]. Upon LMEM convergence, model predictions were plotted against the true value of *jerk*, yielding slope and intercept of the linear regressions as 1.0 and 0.0, respectively, in 98% of subjects. Median(25th,75th) of RMSE were 2.44E-05(8.57E-07, 8.04E-04).

Conclusion:
Lower BGM increase rate and higher jerk were associated with the free-living ambulatory setting. The algorithm characterized the BGM curve for all meals for 500 days depicting the differences for in-hospital (less physical-activity) and ambulatory settings (more physical-activity). LMEMs were able to predict a linear relation between fixed effects and the accelerometer with good accuracy. This method can potentially complement existing techniques to improve glucose control by accounting for physical activity.

Continuous Glucose Monitoring in a 71-year-old Man with Diabetes and COVID-19 During an Episode of Cardiac Arrest, Return of Spontaneous Circulation, and Death

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Objective:
We assessed real-time continuous glucose monitoring (rtCGM) data in an individual with type 2 diabetes who presented with severe symptoms of COVID-19 and suffered a fatal cardiac arrest during hospitalization. We evaluated (1) the utility of using rtCGM in the critical care setting through comparison with venous and point-of-care (POC) glucose measurements and (2) report rtCGM data during the clinical scenarios of cardiac arrest, resuscitation, and death.

Method:
This retrospective analysis utilized rtCGM data (Dexcom G6, Dexcom Inc., San Diego, CA) to evaluate changes in blood glucose levels in a 71-year-old male with COVID-19 symptoms who suffered a fatal cardiac arrest.

Result:
Blood glucose levels remained constant at 220-225 mg/dL after the first cardiac event, slowly decreased to 167 mg/dL after return of spontaneous circulation (ROSC) was achieved, decreased to 141 mg/dL over the first postmortem hour and quickly declined to undetectable levels within the next 20 minutes. Over the course of CGM utilization, the day-weighted percent difference between rtCGM values and venous glucose measurements was 6.7%.

Conclusion:
rtCGM correlated well with venous and point-of-care glucose measurements and was reliably used to manage diabetes in this critically ill patient. Wider adoption of rtCGM may help identify blood glucose patterns and uncover new insights to various comorbidities and conditions.

Web-based Simulation Tool for Self-Management Support in Type 1 Diabetes

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Objective:
To design and implement a novel, user-centric, cloud-based framework that allows people with type 1 diabetes (T1D) to easily explore changes to their individual insulin treatment parameters or measured behaviors.

Method:
Glucose, insulin, and meal records are automatically transmitted from the patient's insulin pump to the Web-based Simulation Tool, also known as WST. Field collected data are processed, including algorithms for mealtime correction/detection, and then fed into a scalable, computing cluster, where the reconstruction-replay engine of WST is personalized. Cleaned data and adjusted model parameters are saved into the system's database on a daily basis. The system is presented to users as a responsive website through which they are able to visualize their data from a particular date range, simulate changes to their insulin parameters and meals, and generate comparison reports.

Result:
The reconstruction-replay engine of WST was evaluated using real data (study ID: NCT02558491) and synthetic data from N=50 virtual subjects that included meals, exercise, insulin sensitivity variability, and sensor noise and calibrations. The median MARD across all experiments was below 11% for both glucose reconstruction and synthetic prediction under basal rate and meal bolus adjustments up to 25%. In terms of error grid analysis (EGA) performance, predictions fell more than 99% of time into the A- and B-zones, confirming that results are clinically acceptable. Usability of WST will be evaluated in a pilot clinical trial under normal living conditions at home.

Conclusion:
Bringing proven simulation technologies to patients with T1D enables unique patient-data interactions that can lead to better diabetes literacy and, ultimately, improved glucose control.

A Data Management Platform for the Assessment of New Type 1 Diabetes Therapies in Clinical Trials

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Objective:
Therapy of type 1 diabetes (T1D) generates a large amount of different data (e.g.: glucose sensors, insulin pumps, meal info and composition, activity trackers, etc.). Effective collection, storing and presentation of such data is essential during clinical trials aimed at testing new therapies. The aim of this work is to present a unified platform able to simultaneously guarantee: security and anonymity of data; data persistence in a structured and standardized format; and modularity needed to implement the new therapies under test.

Method:
The platform is composed by a cloud database, a mobile application, and a web interface. The platform assures the following key features: i) safe communication with continuous glucose monitoring sensors, ii) integration of data generated by common healthcare applications, iii) data privacy and structuring, and iv) real-time patient monitoring. The mobile application is easy-to-use, intuitive, and intended to be used by patients as their diary.

Result:
As a preliminary test of usability, the prototype platform has been used by a volunteer patient with T1D in a short session lasting seven days. The volunteer reported good user experience, that has been further improved with the introduction of data insertion reminders and other features to keep the patient informed about his glycemic control. More intensive testing of the prototype is presently under development.

Conclusion:
The developed platform is potentially useful for data gathering and real-time patient monitoring in clinical trials aimed at testing new T1D therapies.

Cost-Utility of an Online Education Platform and Diabetes Personal Health Record: Analysis over Ten Years

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Background/Objective:
My Diabetes My Way (MDMW) is Scotland's interactive website and mobile app for people with diabetes and carers (currently ~50,000 registrants). It contains multimedia resources for diabetes education and offers access to electronic personal health records. This study aims to assess the cost-utility of MDMW compared to routine diabetes care in people with type 2 diabetes who do not use insulin.

Method:
Analysis used the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model2. Clinical parameters of MDMW users (n=2,576) were compared with a matched cohort of individuals receiving routine care alone (n=11,628). Matching criteria: age, duration of diabetes, sex, and socio-economic status. Impact on life expectancy, quality-adjusted life years (QALY), and costs of treatment and complications were simulated over ten years.

Result:
MDMW cohort: 1670 (64.8%) men; average age 64.3 years; duration of diabetes 5.5 years. Females: average age 61.6; duration 4.7 years. The cumulative mean QALY (95% CI) gain: 0.054 (0.044; 0.062) years. Mean difference in cost: -£118.72 (-£150.16; -£54.16) over ten years. Operating costs of MDMW at the time of analysis were approximately £34.20/registered user/decade, equivalent to a return on investment of well over 3:1.

Conclusion:
MDMW is 'dominant' over usual care (cost-saving and life improving) in supporting self-management in people with type 2 diabetes not treated with insulin. Wider use may result in significant cost savings through delay or reduction of long-term complications and increased life expectancy in Scotland and other countries. MDMW may be among the most cost-effective interventions currently available to support diabetes.

How to Assure Insulin Quality on a Molecular Level by Novel Analytical Methods

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Objective:
Human insulins and their analogs can undergo different degradation processes on a molecular level when exposed to stress conditions, such as temperatures or shear strain, deviating from recommended manufacturer's storage recommendations. These molecular processes lead to a conformational reorganization of the insulin molecules, followed by irreversible agglomeration and fibrillation, most likely accompanied by a decrease in biological potency.

Method:
Infrared spectroscopy offers a reliable approach for quantitative and qualitative insulin monitoring without the application of the sophisticated HPLC reference method, as stated in international pharmacopoeias. A human monocytes cell-based method for the determination of biological potency, using microdialysis and infrared spectrometry, has been tested using a USP insulin standard. Reference measurements for total insulin quantification and formed aggregates were done using a HPLC method, as well as fluorescence and UV/Vis spectroscopy for total protein quantification.

Result:
Changes in the molecular structure of short-and long-acting insulins were observed after several weeks when stored at 37°C. When stored at ambient temperatures or just above 0°C, no significant changes have been found for formulated insulins, but for samples purified by ultrafiltration. An analysis of the insulin`s secondary structure reveals early molecular conformational changes as identified by IR-spectroscopy of dry-film samples. Agglomerates were detected by using a novel HPLC protocol and comparative IR measurements confirming extensive misfolding. Biological potency measurements were carried out using the cellular glucose metabolization rates, correlating with insulin concentrations in the growth medium.

Conclusion:
IR-spectroscopy offer a fast and reliable method for quality assurance and quantification of commercial insulins and could replace the current pharmacopeial methods. In combination with a cell-based biological potency assay, this approach could also meet the USP requirements.

Evaluation of Follow-up Rates in a Large Teleretinal Screening Program

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Objective:
Although sequelae of uncontrolled diabetes mellitus are routinely communicated to patients at office visits, patients seen via telehealth are often lost to follow-up. We performed a retrospective cohort study to determine follow-up rates of patients enrolled in the Grady Hospital's Diabetic Teleretina screening program.

Method:
From 1/18/2018 to 9/28/2018, 6,876 diabetic patients in the Grady Healthcare System were screened for ophthalmologic complications via one of thirteen Teleretina cameras in the Atlanta area. Pathology results were referred to the Grady Eye Clinic (GEC) for evaluation. The study's cohort consisted of patients found to have proliferative diabetic retinopathy (PDR) and/or diabetic macular edema (DME). Follow-up was determined successful if a patient scheduled and showed up to GEC following the screening result. The number of phone calls made by the staff to each patient to schedule appointments was recorded. Initial recommendations provided to the patient at the first GEC appointment were used to track patient adherence to treatment plan.

Result:
N=269 patients were diagnosed with PDR and/or DME via Teleretina screening. Eyes were tracked individually. 369 of 538 eyes made it to the first GEC visit, yielding a 68.9% follow-up rate. Over half (55%) of patients completed initial treatment recommendations. Average time from screening to first visit was 46.1 days. Almost three-fourths (72.7%) of patients showed up to GEC after receiving one scheduling phone call from staff, 54.7% after two calls, and 44.4% after three calls.

Conclusion:
The Grady Teleretina Screening Program successfully set up appointments within two months for nearly 70% of patients with PDR and/or DME. Over half (55%) completed initial treatment recommendations. However, a significant portion of patients remained lost to follow-up. Additional attempts to contact patients displayed diminishing returns. Further studies should investigate barriers to care following telehealth screening.

Diminished Weekday/Weekend Differences in Glycemic Control in the COVID-19 Pandemic

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Objective:
Behavioral changes associated with the COVID-19 pandemic may influence diabetes management decisions and glycemic control among users of continuous glucose monitoring (CGM) systems. We sought to examine the effects of the pandemic on CGM metrics that typically differ between weekends and weekdays.

Method:
Data were from a convenience sample of 4,703 users of the G6 CGM System (Dexcom, Inc., San Diego, CA) with postal codes in either New York City (New York), Los Angeles County (California), or Cook County (Illinois) and were required to have uploaded at least 70% of possible glucose concentration values between 01-01-2020 and 06-20-2020. Pre-pandemic and late-intra-pandemic intervals were defined as 01-01-2020 to 03-01-2020 and 04-20-2020 to 06-20-2020, respectively. Weekends were Saturdays and Sundays; other days were weekdays. Time in range (TIR) was defined as the percentage of glucose values in the 70-180 mg/dL range. Glycemic variability was calculated as coefficient of variability (CV). Paired t-tests were used to compare the changes in daily % TIR and CV, before and during the pandemic.

Result:
Before the pandemic, weekends were characterized by significantly lower mean±SD TIR values than weekdays (58.3± 26.6 vs. 59.5± 26.5%, respectively, $p<0.001$). During the pandemic, weekend TIR improved to 61.6% and weekday TIR improved to 62.2%. The magnitude of the weekend/weekday TIR discrepancy decreased from 1.2 ± 6.2% pre-pandemic to 0.6 ± 5.6% intra-pandemic, $p<0.001$. Before the pandemic, weekend and weekday CV's were 29.3% and 28.7%, respectively; these fell to intra-pandemic levels of 29.0% and 28.5%.

Conclusion:
Early stages of the COVID-19 pandemic were associated with significant improvements in TIR, as well as with a decrease in TIR differences usually seen between weekends and weekdays.

Individualized Linear Models for Glucose Prediction: Parametric *vs.* Non-Parametric Identification

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Objective:
Accurate personalized models of glucose-insulin dynamics can be extremely useful in improving methods to forecast glucose concentration, thus permitting more effective and proactive glucose management. Here, exploiting information on injected insulin, carbohydrate intake, and past glucose samples, we investigated and compared the performance of two different approaches for, in particular, linear black-box model identification of such models: parametric *vs.* non-parametric.

Method:
For the parametric approach, that restricts the search of the system dynamics to a finite-dimensional set of functions parametrized by a parameters vector, we derived individualized linear predictors using the Prediction Error Method (PEM), the state-of-the-art identification technique, and the most general model parametrization (Box-Jenkins). For the non-parametric approach, we implemented *ad-hoc* code solving an optimization problem in an infinite-dimensional functional space known as reproducing kernel Hilbert space. Both approaches were used to identify a model for N=11 real subjects. Model performance was assessed by computing Coefficient of Determination (COD) at different prediction horizons (PH), and the results were compared using ANOVA.

Result:
Non-parametric models grant an improvement of COD of about 2%, 7%, 21%, and 41% for, respectively, a PH = 30, 60, 90, and 120 min. The paired-sample *t*-test confirms that the prediction accuracy is significantly different for PH=30, 60, and 90 min (p-value≤0.001, p-value=0.003 and p-value=0.03 respectively), while for PH=120 min, p-value=0.07.

Conclusion:
The use of a non-parametric approach grants statistically significant improvement to prediction accuracy with respect to the state-of-art parametric approach. Notably, the so-identified personalized models can also be used as core of model-based control techniques, such as Model Predictive Control, to design personalized automated insulin delivery systems.

Simulation Platform Development for Diabetes and Technology Self-management

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Objective:
We aim to: (1) test the usability and acceptability of a diabetes self-management and technology education simulation platform, and (2) develop a monitoring function by which diabetes device data is used to assess needs and personalize education.

Method:
Thirteen rural adult insulin pump users with T1D participated in a mixed methods usability study. Participants navigated 3 simulations (i.e. site occlusion, hypoglycemia, exercise) using a virtual insulin pump built into the web-based platform. Testing was initially done in clinic but converted to virtual in response to COVID-19 restrictions. Diabetes devices were downloaded to evaluate associations between platform performance and personal device data. A Synthetic Minority Oversampling Technique was used to fit predictive models and decision trees were used to visualize patterns leading to good or poor simulation performance. Semi-structured interviews examined recurring themes reflecting usability and acceptability.

Result:
Participants were 28-70 (mean 51.3) years old, 77% (10/13) used automated insulin delivery devices, and 92.3% (12/13) used continuous glucose monitoring. Mean Net Promoter Score of 9.5 (range 9-10) and positive sentiment during interviews indicated very high acceptability. Systems usability scale (mean 88.5, range 70-100) indicted a high degree of perceived usability. Self-monitoring blood glucose/frequency >4.4, bolus/frequency >5.4 and Diabetes Knowledge-2 Insulin Sub-section score >9 predicted successful site-occlusion scenario performance with an 80% accuracy. Round 1 modifications included glucose meter addition, playback button, algorithm adjustments, and avatar upgrades to address platform confusion and functionality issues. Modifications suggested from round 2 included: virtual CGM, additional content library, personalized content, and brand specific devices.

Conclusion:
Virtual simulation platforms show significant potential to increase access and frequency of self-management and technology education. Additional study is needed to determine sustained engagement and the benefit associated with simulation education technologies.

Insulin Transition Calculator: A Safety Evaluation

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Objective:
Previous studies demonstrated improved glucose control and less hypoglycemic events using a standardized protocol when transitioning from intravenous (IV) infusion to subcutaneous (SQ) insulin. A calculator was developed at UCSD Health to assist with insulin transition by providing SQ recommendations based on infusion requirements, diabetes history, and nutrition. Prior to integration with the electronic health system, this has primarily been available to pharmacists and trialed by few providers. The goal was to determine whether this is a safe application for all physicians to utilize.

Method:
A single-center, retrospective assessment was performed of hospitalized patients between October 2019-April 2020 in whom insulin transition was ordered using the transition calculator. First, patient charts were reviewed for the accuracy of the physician-inputted data. Then, the total daily dose (TDD) of SQ insulin was compared between calculator recommendation versus ordered dose. The primary safety outcome was incidence of hypoglycemia within 48 hours of transition.

Result:
Of n=24 patients, 8% (n=2) experienced hypoglycemia (BG <70 mg/dL). One event was secondary to insulin:carbohydrate mismatch by the nurse. The other was due to high-dose steroid discontinuation following transition. Overall, the calculator recommendations were on the conservative side, as more patients experienced hyperglycemia when the TDD was within 10% of the calculator's recommendations (80%) compared to TDD greater than 10% of the recommendations (40%). The exception to this was a patient on high-dose steroids, which caused artificially elevated TDD recommendations.

Conclusion:
Excluding patients on steroids, the insulin transition calculator recommendations were conservative and responsible for zero hypoglycemic events. Therefore, we believe this application may be applied safely by all providers following education on nutrition input and limitation in the setting of steroid use.

Reversing Prediabetes Diagnoses with Sustainable Lifestyle Intervention

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Objective:
To improve the lives of people diagnosed with prediabetes or type 2 diabetes through scalable digital health coaching.

Method:
Patients who had been diagnosed with prediabetes or type 2 diabetes were provided access to a digital health program and a personal health coach. The multi-disciplined health coaches included qualified and registered dietitians, trainers, physiotherapists and nutritionists who provided tailormade guidance, support and empathy, through video and text to help patients tackle or prevent type 2 diabetes. Patients could log and track multiple health goals including exercise, diet, mood, medicine, weight, blood pressure, and sugar levels, which can then be monitored by their personal coach. Over a 12-month program, the aim was to lower the weight of obese patients and reduce A1c levels for patients living with prediabetes or type 2 diabetes.

Result:
Real-world data across Liva's population, a combination of randomized controlled trials (RCT) and observational studies, showed that:

- 38% of people with obesity on the program had sustained a weight loss of 5% of their body weight at 12 months.
- 47% of people on the program living with prediabetes normalized their long-term blood sugar below the threshold for prediabetes.
- 80% of people on the program living with prediabetes sustained a reduced A1c at 12 months.
- Average bodyweight reduction of 6.3% after nine months among people on the program living with type 2 diabetes, corresponding to an approximate 20% reduction in societal costs.

Conclusion:
By giving people access to a digital health coach, patients with prediabetes or type 2 diabetes are able to dramatically improve their health. A single health coach can supervise up to 500 patients per year, making this a scalable solution for healthcare providers.

Maximizing IV Insulin Safety and Outcomes for Inpatients with COVID-19: eGMS Availability & Protocol Adjustments

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Objective:
Poor inpatient glycemic management worsens outcomes for patients with COVID-19. Managing hyperglycemia amid challenges of bed, staffing, and PPE shortages is complicated by the hourly glucose checks required by most IV insulin protocols. The purpose of this study was to review the impact of a support kit provided to accommodate care modifications for inpatient glycemic management in the COVID-19 inpatient population.

Method:
All clients using an IV electronic glycemic management system (eGMS) received a Diabetes and COVID-19 Support Kit with current pandemic resources and were also offered an opportunity to quickly expand the eGMS availability in units needed to meet surge demands. The Kit provided guidelines for changing parameter settings to safely achieve blood glucose levels of < 180 mg/dL while transitioning to 2-hour glucose check once patients were within goal range. A survey was distributed to hospital systems that deployed a component of the support package.

Result:
Thirty percent of targeted hospital systems completed eGMS unit expansions increasing availability to 3,277 more beds. Fifteen hospital systems returned the survey. All survey respondents had treated COVID-19 patients and were concerned about conserving PPE and the exposure risk associated with frequent glucose checks. Four-fifths (80%) of respondents felt eGMS helped them better manage COVID-19 patients with diabetes; 4 hospital systems reported some adjustment of parameters. Only 1 hospital system had used CGM in the previous months and only as a trial utilization for tracking glucose variability.

Conclusion:
Further collaboration with clients regarding the COVID-19 parameter settings adjustments is ongoing to assess the impact on workflow and patient outcomes. Subsequent studies of sites that made parameter changes will enhance support opportunities in the ongoing COVID-19 response.

The Extended Wear Infusion Set – A Design for Plastic Waste Reduction

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Objective:
Most insulin pump therapies require frequent insulin infusion set changes to avoid events such as skin irritation, infection, occlusion, or set loss at the infusion site. This, in combination with the single-use medical device model that lowers the risk of infection and/or injury, can contribute to a considerable amount of plastic waste. This study compared the environmental impact of the Medtronic 7-day Extended-Wear Infusion Set (EWIS) to that of current on-the-market serter-incorporated infusion sets.

Method:
The average amount (kg/year) of disposed plastic (i.e., the cannula, hub, tubing, cap, disconnect cover and disposable serter) at the end of the labeled product service life of six serter-incorporated infusion sets with different tubing lengths (i.e., the MiniMed™ Mio™ and Tandem Autosoft™ 90 [24 to 25 g/each], Mio™ 30 and Tandem Autosoft™ 30 [21 to 22 g/each], Mio™ Advance [21 to 23 g/each] and EWIS [22 to 23 g/each]) was determined and compared.

Result:
Plastic waste was reduced by an average of 1.5 - 1.9 kg annually by using the EWIS in place of Mio™ and Autosoft™ infusion sets. In aggregate, the EWIS is estimated to reduce overall plastic waste by over 496 metric tons/year.

Conclusion:
The use of a 7-day EWIS substantially reduces plastic waste compared to a 3-day wear serter-incorporated infusion set, resulting in a more environmentally sustainable option for infusion sets.

Use of a Mobile Platform to Improve Diabetes Management in Adolescent Type 1 Diabetes Patients: A Pilot Study

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Objective:
POPS!one is a mobile platform designed to simplify diabetes self-management. The platform integrates a self-contained glucose meter and test modules with an interactive mobile application with results automatically accessible for remote clinical review. Preliminary testing validated accuracy of blood glucose (BG) measurements and a less painful lancet experience compared to traditional devices. We examined the impact of sustained use on A1c, test frequency, and average BG.

Method:
Fifty-one adolescent injection-users with T1D were enrolled into a prospective, single arm, clinical trial and used POPS!one for 6 months with follow-up at routine quarterly visits. Differences between A1c, average BG, and test frequency at baseline and 6 months were compared using generalized mixed effects regression.

Result:
Overall, N=20 patients completed the study, with N=31 patients not completing the study (withdrawal, failure to meet minimum test requirements, lost to follow up). Among the completers, 65% were male and 90% White/Caucasian; average age was 15.8±2.9 years, with a mean T1D duration of 5.6±3.6 years. Average A1c improved significantly from 8.97±0.65% at baseline to 8.50±0.98% at 6 months (p-value=0.0052). Of the completers, there were no demographic or baseline clinical data that predicted improvement in A1c. Given the attrition rate, completers and non-completer populations were compared; at baseline, completers had lower A1c (8.97 +/-0.65 v 9.49 +/-0.8, p-value = 0.0128) and lower average BG (204 +/- 44 v 237 +/-47, p-value = 0.0178) with no statistically significant differences between groups in average BG testing frequency during study participation.

Conclusion:
Our findings suggest that sustained use of POPS!one supports diabetes management with significant improvement in A1c. Future research of the platform will include assessment of long term utilization and quality of life metrics.

Highly Miniaturized, Low Power CMOS ASIC for Long-Term, Needle-Implantable CGMs

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Objective:
This objective of this work is to develop a highly miniaturized, needle implantable, biosensing platform for a continuously glucose monitoring (CGM) system. The biosensing platform for the CGM system comprises glucose sensing elements with custom developed application specific integrated circuit (ASIC) chip, fabricated using 65 nm CMOS technology geared to reduce both size of the implant and its power requirements. The reduced power of the chip on the implant system provides improved coupling with solar power together with longer battery life for the external proximity communicating device.

Method:
The electrochemical glucose biosensors under development at Biorasis/UConn were integrated with a 65 nm CMOS signal processing chip. This chip interacts with the glucose sensing electrodes and transmits digital pulses optically through the skin to the proximity communicator. Integrated devices were tested *in vitro* between 2 mM and 25 mM glucose.

Result:
The device platform demonstrated a linear response (R^2=99.5) to glucose challenges with a sensitivity of 1278 Hz/mM. The ASIC CMOS chip has a small physical footprint (0.45 mm × 1.2 mm). This chip, integrated with biosensor platform and opto-electronic components, had an overall power consumption ~60 μW.

Conclusion:
The miniature footprint of the biosensor platform, together with its low power consumption, renders this a versatile platform for minimally-invasive, fully-implantable, real-time CGM. This platform is small enough to be inserted in the subcutaneous tissue through a 14-gauge needle. This system is intended to improve the quality of life for patients with type 1 and type 2 diabetes. The development of the 65 nm CMOS chip was supported by US Army and clinical translation was supported by Helmsley Charitable Trust.

Performance of the GLUCOCARD Shine Blood Glucose Monitoring Systems Throughout Shelf-Life

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Objective:
Blood Glucose Monitoring Systems (BGMS) need to provide accurate results throughout their product life cycle. ARKRAY employs rigorous quality testing programs for the release of new test strip lots and evaluates a sampling of lots over the entire product life cycle, including expiration. Currently, FDA 2016 over-the-counter accuracy criteria is the most stringent for self-monitoring blood glucose systems. The accuracy boundaries for this standard require 95% of BGMS results to be within ±15% of the reference analyzer and 99% of BGMS results to be within ±20% of the reference analyzer.

Method:
Seven lots of GLUCOCARD Shine test strips are currently being evaluated or have been evaluated at the ARKRAY laboratory in our on-site IRB approved clinical study. Four lots are in the process of being tested while three lots have been tested through the product shelf-life (i.e., 24 months) and post-expiration (up to 32 months). Our on-site clinical testing includes capillary blood sampled from the fingertip of people with diabetes (n=30 at each time point) by laboratory professionals for a total n=929 samples. Reference values were obtained using the YSI Model 2300 Analyzer. Data were analyzed against FDA 2016 over-the-counter accuracy standard. Average bias throughout shelf-life and 95% Confidence Intervals (CI) were calculated.

Result:
A total of 96.9% (900/929) of results were within ±15% of reference and 99.1% (921/929) of results were within ±20% of reference. Average bias within shelf-life, throughout shelf-life, and post-expiration for all lots combined was 1.13% [95% CI of 0.72% to 1.53%].

Conclusion:
Data collected on the GLUCOCARD Shine BGMS platform performed within the accuracy boundaries of the 2016 FDA over-the-counter accuracy standard and demonstrated consistent performance throughout its product life cycle.

Radiometer ABL90 Flex Blood Gas Analyzer versus YSI 2300 Stat Plus Method Comparison

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Objective:
Blood gas analyzers have the potential to replace the YSI 2300 Stat Plus as a glucose reference analyzer following discontinuation of the device in 2021. Testing documented here assessed the glucose performance of the Radiometer ABL90 Flex against the YSI 2300 on samples collected from people with and without diabetes. Method comparison analyses were carried out to determine the suitability of the ABL90 Flex as a glucose reference analyzer.

Method:
Three ABL90 sensor lots were tested alongside the YSI 2300 in Arkray on-site clinical and in-house capillary testing. Arkray on-site clinicals test capillary whole blood sampled from the fingertip of people with diabetes by laboratory professionals (n=174; 29 donors, tested in duplicate, at 3 time points). In-house capillary testing consisted of capillary whole blood sampled from the fingertip of people without diabetes by laboratory professionals (n=60; 15 donors, tested in duplicate, fasting and postprandial states). ABL90 testing utilized capillary whole blood, and YSI 2300 testing utilized capillary plasma. One ABL90 sensor cassette was excluded from dataset due to solution pack issues. Data were analyzed using difference plots [median bias and quantile limits of agreement (LoA)] and weighted Deming linear regression with all associated statistics reported.

Result:
No statistically significant differences were found between ABL90 and YSI 2300 glucose data. Weighted Deming linear regression equation: [ABL90] = 0.8676 + 0.9902[YSI 2300]. Intercept: 95% CI: -2.451 to 4.186; p-value 0.6056. Slope: 95% CI: 0.9662 to 1.014; p-value 0.4218. Relative difference plot median bias of -0.64% [95% CI: -0.976% to 0.000%] with LoA -4.81% [95% CI:-5.515% to -4.367%] to 5.11% [95% CI: 3.774% to 20.408%] with 95.7% of results within LoA.

Conclusion:
Data presented here show adequate agreement between ABL90 and YSI 2300.

The Effect of a Digital Therapeutic Platform on Glycemic Control in Adults above Age 65 with Type 2 Diabetes

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Objective:
A commonly held belief is that older adults may not be technically savvy enough to benefit from digital therapeutics. The present study examines whether the Dario digital therapeutic can contribute to better diabetes management in adults above age 65. Dario digital therapeutic solution consists of a mobile application, coaching, and glucometer integration.

Method:
A population of 12-month Dario active users with type 2 diabetes, non-insulin treated, whose first-month blood glucose average was greater than180 mg/dl, was evaluated. Clinical outcomes included average blood glucose, ratio of very high readings (>250 mg/dL) per total measurements and the percentage of population that reduced their average blood glucose below 169 mg/dL (equivalent to A1c 7.5% the glycemic goal for older adults according to American Diabetes Association). Users were stratified into two groups: one age group ≥65 years and second age group <65 years.

Result:
Users in age group ≥65 (N=298) improved their average blood glucose at six months by 13% (187±38 vs. 214±50mg/dL) and sustained outcomes for 12 months (12 month average blood glucose =184±37mg/dL). This observation was comparable in age group <65 at 12 months (N=642) (195±36 vs. 221±52mg/dL). High readings ratio (>250 mg/dL) was reduced in age group ≥65 by 38.1% at six months and by 41.5% at 12 months. The ratio of high readings in age group ≥65 was significantly lower than in the age group <65 at 12 months (13.7% vs. 20.6%). 47% of users in age group ≥65 (140 out of 298) reduced their average blood glucose below169mg/dL at 12 months.

Conclusion:
Older adults using a digital therapeutic platform, have the potential to promote behavioral modification and enhance adherence to diabetes management, demonstrating better glycemic control.

Glycemic Response to Athletic Competition Stress

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Objective:
The objective is to understand the glycemic impact of athletic competition stress and to identify factors that make an individual more likely to observe this phenomenon.

Method:
Recreational athletes with type 1 diabetes were recruited for a total of N=7 runners (5M/2F) in 9 races. Participants completed in athletic competition and in a training run at race-pace for a shorter duration and without the stress of the race. The athletes were requested to match, as closely as possible, their carbohydrate and insulin intake prior to both events.

Result:
The area under the CGM curve (AUC-CGM) for training increased with increasing anxiety-proneness measured by the State Trait Anxiety Inventory, STAI–T ($r=0.84$, $p=0.004$). The difference in AUC-CGM between these sessions decreased with increasing STAI–T scores with lower STAI-T individuals observing a larger difference between competition than training ($r=-0.73$, $p=0.03$). In 6/ 9 sessions, we observed a larger AUC-CGM for the race compared to training and those sessions corresponded with lower STAI-T score individuals. The higher STAI-T individuals frequently experienced hyperglycemia in both sessions. The time in each glycemic range was generally less favorable during the race with more time spent below 70mg/dL and above 250mg/dL. The participants with longer duration of diabetes often took more insulin with their carbohydrates on race day than on the training day while the reverse occurred in newly diagnosed athletes ($r=-0.69$, $p=0.04$).

Conclusion:
Competition stress may lead to an elevated glucose trend compared to a training exercise at the same intensity in less anxiety-prone individuals - those less likely to be stressed in non-competition events. With increasing duration of diabetes, experienced athletes might anticipate this phenomenon and, therefore, take preventative measures such as injecting more insulin with carbohydrates during the pre-race time period

Evaluation of Twitter as an Educational Tool for Diabetes Self-Management Using the AADE7™ Framework

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Objective:
Using social network analysis to categorize diabetes self-management (DSM) information on Twitter against seven categories from AADE7™ guidelines

Method:
The study design included retrieving tweets and social network diagrams using NodeXL. Twitter data were collected over a period of 14 days in March 2020. The word diabetes was added to each of the AADE7 self-care behavior terms to be used as a composite search term (For example, diabetes + monitoring = diabetes monitoring). We extracted the tweets and the type of network. Parameters such as vertices (v), edges (e), top influencers, URLs, kinds of users, and top keywords were compared among the seven categories.

Result:
A social network analysis using the seven AADE7™ categories revealed that all seven exhibited a broadcast type of social network. There were stark differences in frequency of AADE7™ term usage, types of influencers, and themes that emerged. “Diabetes monitoring” was the most common self-care behavior mentioned on Twitter (vertices=312, edges=471), followed by “diabetes healthy eating” (vertices=194, edges=188). Further, “healthy coping” (vertices 6, edges= 6), was the least common self-care behavior mentioned on Twitter followed by “Problem Solving” (vertices 13, edges= 15).

Conclusion:
A broadcast type network indicates powerful agenda setters and conversation starters on Twitter for all seven AADE7™ categories. Specifically, “Diabetes Monitoring” included keywords such as telemedicine, URLs such as eBay, and involved influencers such as the President of the United States and a physician who had been in a legal and social media controversy with him. Further, this study indicates that exact terms such as “healthy coping” and “problem solving” might be underrepresented on Twitter in the context of diabetes.

Predicting Blood Glucose Levels Using CNN-LSTM Neural Networks

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Objective:
In this work, a convolution neural network–long short-term memory (CNN-LSTM) architecture was exploited to predict the blood glucose (BG) levels for a 30-60-90 minutes prediction horizon (PH) based on a multivariate physiological dataset of type 1 diabetes (T1D) patients.

Method:
Under the aegis of the research project DIAdvisor™, data were collected from N=59 T1D patients (37 Male/22 Female, mean age: 43.4±11.7 [yr], disease duration 18.8+10.7 [yr], BMI 23.9±2.4 [kg/m^2], A1$_c$ 7.8±1.6 [%], 27 MDI and 32 CSII) participating in a 3-days in-hospital study. Patients were served standardized meals for breakfast, lunch and dinner (carbohydrate content: 42, 70, 70 [g], respectively) and decided insulin needs based on their personal blood glucose meter. The dataset included: interstitial glucose [mg/dL] measured by Abbott Freestyle™, insulin intake [u] for basal, bolus and corrections, and meal nutrient content [g] for carbohydrate, protein and lipids. After preprocessing, the dataset was divided into 80% for train/validation and 20% for testing, respectively without randomization, to ensure that no information from the test patients was included in the training process. Then train/validation set was randomly divided into 80%-20%. A CNN-LSTM network was trained for 200 epochs with batch size of 128 (1s and 7ms per epoch).

Result:
Evaluating the model performance in predicting the CGM for patients in the testing set resulted in mean absolute error (MAE) of 6.49, 12.9, 27.52 [mg/dL], and root mean square error (RMSE) of 9.9, 19.9, 32.1 [mg/dL] for 30, 60, and 90 minutes PH, respectively, which, to our knowledge, are among the best performing for specifically 90 minutes PH.

Conclusion:
For people with T1D, accurate forecasting of BG levels would effectively avoid hyperglycemia and hypoglycemia. The proposed approach, based on a CNN-LSTM model, reliably predicts retrospective clinical blood glucose data both in the short- and long-term, yielding superior performances.

Painless Insulin Delivery Through the Skin based on Sonophoresis (Ultrasound)

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Objective:
There is a need to develop new ways of administering insulin that can increase the patient's quality of life and adherence without decreasing the efficacy of the therapy. Medicsen is testing an insulin administrator based on sonophoresis to ensure the painless and effective transdermal delivery of insulin.

Method:
Sonophoresis and transdermal insulin delivery was tested both *in vitro* and *in vivo* over two years to prove safety and efficacy. (Permeability studies were used to prove efficacy as well as safety studies for insulin and the skin).

Result:
All tests produced positive results indicating the lack of damage to both the insulin molecule, which maintains its biological function and stability as seen *in vivo* and in HPLC studies or in the circular dichroism spectra obtained from the Lantus Insulin solution treated with the technology, finding no variability among the samples evaluated (n = 7), reaching the characteristic minimum at 219 nm (sd +/- 8.31) in both experimental and control groups. Skin tests of sonophoresis showed no significant damage as demonstrated by electronic microscopy evaluation of the skin or by ELISA in which changes in the expression and concentration of relevant skin cellular compounds such as TNF α and IL-2. Lastly, the technology proved to be effective in the delivery of insulin molecules through the skin in a non-invasive way, as observed in a Franz Diffusion Cell system, and by the reduction of blood glucose *in vivo*.

Conclusion:
All evidence collected during *in vitro* and *in vivo* studies shows promising results, indicating that the technology developed by Medicsen is safe and effective. As a result, human trials will be performed in order to fully demonstrate its potential for the treatment of diabetes.

Persistent Hyperglycemia in Extremely Low Birth Weight Premature Infants

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Objective:
Hyperglycemia, high blood glucose (BG), is very common in very/extremely premature infants due to stress and metabolic prematurity, and is associated with increased mortality and morbidity. STAR-GRYPHON is a model-based decision support system for insulin dosing in the neonatal intensive care unit since 2013 in Christchurch. This study examines model-based glycemic control outcomes against a retrospective cohort to assess trends in delivery, quality of control, and metabolic physiological response.

Method:
Retrospective analysis of glycemic control outcomes from STAR-GRYPHON (January 2013-2019, n=59 episodes, 4929 hours) was compared to a 2008 cohort (n=25, 2946 hours) treated with a sliding-scale insulin protocol. STAR-GRYPHON control was compared yearly to discern trends in delivery and physiology. Glycemic control outcomes were assessed by percentage (hourly-resampled) BG >180mg/dL, percentage BG in 72-144mg/dL range, and percentage BG less than 72 mg/dL.

Result:
STAR-GRYPHON had lower BG (Median [IQR] BG 130 [112-153]mg/dL vs. 142 [119-166]mg/dL), greater time in target range (66% vs. 52%), less hyperglycemia (9.6% vs. 16.4% BG >180mg/dL), and lower incidence of mild hypoglycemia (0.46% vs. 2.1% BG<72mg/dL) compared to retrospective care.
Time in range was highest in 2013 (76.6%), decreasing over 5 years due to persistent early hyperglycemia in some patients. Persistently hyperglycemic infants received insulin doses comparable to the adult saturation range (0.09-0.2 U/kg/hr) - indicating an upper limit of the insulin effect, and had lower weight and gestational age.

Conclusion:
Infants under STAR-GRYPHON are increasingly more insulin resistant over a 6-year study period. Insulin saturation and subsequent hyperglycemia, as evidenced in the data and trends, limits overall control performance, and indicates the need to restrict nutritional intake if BG normalization for all patients is desired.

Measuring Metabolic Impact and Recovery in Endurance Athletes Using CGM

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Objective:
Exhaustive endurance events incite significant metabolic impact. One major objective in the sporting industry is to accurately monitor athlete recovery to optimize training efforts and event performance. Continuous glucose monitors (CGMs) provide frequent, minimally invasive, blood glucose (BG) measurements, which can potentially capture the metabolic impact and trajectory of a major endurance exercise event and subsequent recovery. This study tests this hypothesis using data from sub-elite athletes.

Method:
Ten (N=10) sub-elite athletes were recruited and fitted with CGM devices. BG was monitored for 4-6 days. All nutrition and exercise inputs were recorded. Athletes performed an endurance exercise test to exhaustion after 1-2 days of monitoring after a prior rest day. Validated State and Substate pattern analyses quantified glycemic levels and variability before and after the exercise test, overnight basal glucose behaviors, and BG response to carbohydrate intake.

Result:
Overall glycemic variability increased from the 80th percentile on the day of the test and returned to baseline (day prior) levels the day after the test. Overnight BG remained elevated up to 3-4 days post-test with an average increase of 16% compared to the night before the test. Metabolic variability in response to carbohydrate intake was increased from the 60th percentile upwards on the day of the test, returning to baseline pre-test levels the day after. These results capture the metabolic impact of the test and subsequent recovery.

Conclusion:
The initial hyperglycemic post-test period and lasting metabolic impact of an endurance test to exhaustion are quantifiable in commercially available CGM devices. These results encourage further investigation into using CGMs to monitor athletic recovery after intense endurance exercise events based on their impact on glycemic levels and variability.

Unannounced Meal Management within the DBLG1 System

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Objective:
The objective is to implement an Unannounced Meal Management (UMM) feature that would detect and manage any unexpected sudden increase of blood glucose in a safe and efficient way.

Method:
The method involves three stages: 1) a meal estimation, 2) a detection module and 3) a computation of the insulin required to offset the estimated meal. The controller was evaluated *in silico* with and without the activation of the UMM feature, using a simulator based on the Hovorka model involving N=120 virtual patients. Various meal scenarios were considered with different levels of meal announcement ranging from 0% to 100% meal announcement, where an announced meal produces a bolus delivered a few minutes ahead of the meal declaration time.

Result:
The simulation results showed a time in range [70-180 mg/dL (TIR)] improvement of 5% without increasing the hypoglycemia rate (<70 mg/dL) when the UMM feature is active in a full unannounced meal (FUM) scenario. Results in a full announced meal (FAM) scenario also reveal that the UMM feature did not increase hypoglycemic risk significantly while leading to a slight TIR improvement (~0.5%) that can be imputed to unexpected glycemic excursions not related to meal intake, yet covered by the UMM module. These figures also show that the UMM controller approached, in the FUM scenario, the performances obtained in the FAM scenario with the reference controller: the TIR is only <5% lower (56.51% with UMM in FUM vs. 61.94% with reference in FAM).

Conclusion:
The new UMM module was assessed *in silico* to be safe and effective and could be evaluated in a real-life clinical trial.

The Smartphone as a Complete Device for Diabetic Telehealth in COVID19

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Objective:
The objective is to find smartphone features and free apps to provide care to our diabetic patients in the COVID-19 and shelter in place restrictions.

Method:
We assessed the most popular downloaded communication apps in Droid and iOS app stores and pertinent smartphone features for diagnosis.

Result:
In the first half of 2020, Apple and Google app downloads have increased by 22.8% and 27.3%, respectively Communication: Top 10 free Android apps: 1) Skype, 2) Zoom, 3) RingCentral, 4)V-see, 5) Vidyo 6) Telehealth by Simple Practice 7) Medici: Video chat 8) eVisit Telehealth 9) Jiyyo: A TeleHealth Platform for Doctors 10) DocsInc. Downloads range from 1 billion for Skype to 1000 downloads for DocsInc. Top 4 free iOS apps: 1) Skype, 2) Zoom, 3) Telehealth by Simple Practice 4) Medici. Built-ins: Facetime (iOS), Google Duo (Android)
Diagnosis: Smartphone features for telehealth:
Imaging (Camera)
1. Black and White = infrared imaging for skin lesions for dermatology consultation
2. Color photos: documentation of foot ulcerations, pressure ulcers by patients, skin infections, gum infections, cellulitis, color photos of eye infections.
3. Measurement: built-in iOS app “Measure” for lesion size (Augmented reality)

Conclusion:.
As physicians facing the challenges of remote care, the smartphone built-in features can be further explored for patient care.

A Massive Open Online Course for Type 2 Diabetes Self-Management: Adapting Education in the COVID-19 Era

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Objective:
Type 2 diabetes self-management education is an essential component of type 2 diabetes care that is traditionally delivered in a face-to-face setting. In response to the COVID-19 pandemic, innovative solutions are urgently needed, allowing provision of self-management education that can be delivered in compliance with social distancing policies. Innovations that are self-service, and that can deliver education efficiently at low cost, are particularly appealing to healthcare providers and commissioners.

Method:
We developed and evaluated a free massive open online course in diabetes self-management education created and delivered during the COVID-19 pandemic. This course made use of online interactive content including expert and patient videos, quizzes, moderated discussion boards and live social media which encouraged personal reflection and goal setting. User expectations and experiences were explored via survey-based methods.

Result:
N=1991 users registered interest in the course over a 2-week period, with N=976 users starting the course and N=640 (65.6%) users completing the course in full. Participants included people with type 2 diabetes (66.5%), people at risk of type 2 diabetes (2.6%), family members or caregivers of people with type 2 diabetes (5.3%), and healthcare providers (28.8%). Users engaged well, finding the course educational, user-friendly, and motivating, demonstrating high completion rates and user satisfaction. A statistically significant ($p < 0.001$) increase in both self-reported self-management ability and health knowledge was observed among participants with type 2 diabetes.

Conclusion:
Massive open online courses in type 2 diabetes self-management education have great potential for delivering education efficiently at scale and low cost. Although engagement can be limited by digital literacy, benefits include flexible and remote access to up-to-date, evidence-based, education delivered by a multidisciplinary team of healthcare providers.

Benefits of the Digital Insulin Titration Application, My Dose Coach, for Individuals with Type 2 Diabetes in Mexico

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Objective:
My Dose Coach (MDC), an FDA-approved smartphone application for individuals with type 2 diabetes, uses patient-recorded fasting blood glucose (FBG) data to provide basal insulin (BI) dose adjustments according to a healthcare professional-prescribed titration plan. This study investigates the impact on FBG reduction of MDC-recommended BI adjustments.

Method:
Of N=411 registered MDC users in Mexico, N=278 individuals recorded ≥2 FBG readings over a 2-week period. N=218 (78.4%) reached individualized FBG targets and were included in outcomes analysis. Users were stratified as having decreased (N=22), increased (N=91), or maintained (N=99) BI dose; N=6 could not be classified.

Result:
Mean ± SD baseline FBG was 148.8 ± 65.7 mg/dL, age was 51.8 ± 12.5 years. Most participants (63%) were receiving U-300 glargine (Toujeo®) versus U-100 glargine (Lantus®) (37%). By the end of the study period, FBG decreased by 26% and mean time to target was 14.7 ± 16.0 days, with 0.3 ± 0.8 hypoglycemic events per participant. Mean BI dose increased from 28.1 to 31.2 U (+10%). The dose increase subgroup had higher initial FBG (190.5 ± 75.2 mg/dL), and greater FBG change (-39%) reached in 23.1 ± 18.0 days compared to the stable dose (baseline FBG, 123.1 ± 33.0; FBG change, -12%; time to target, 7.6 ± 10.3 days) and dose decrease subgroups (baseline FBG, 97.8 ± 39.3; FBG change, +8%; time to target, 10.6 ± 5.6). Hypoglycemic events per participant in each subgroup were 0.1 ± 0.3, 0.1 ± 0.5, and 1.7 ± 1.6, respectively.

Conclusion:
MDC, a digital titration solution for end-user health management, may help users to reach FBG targets with relatively low hypoglycemic risk by providing FBG-based BI adjustments.

Effects of Exogenous Insulin Input on Identification of Hepatic Clearance Parameters

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Objective:
Many metabolic tests require accurate identification of patient-specific parameters from data. Insulin assays are often used to identify insulin kinetics parameters, such as general and first-pass hepatic clearance values. This study assesses if adding small intravenous insulin doses in clinical tests yields more precise identification of insulin kinetic parameter values.

Method:
Insulin and C-peptide data from two intravenous glucose tolerance test trials of healthy adults (N=10x2; denoted A and B), with insulin modification (A) and without an insulin bolus (B), were used to identify insulin kinetics parameters using a grid search. Monte Carlo analysis (N=1000) quantifies the variation in identification error for insulin assay errors of 5%. A region of parameter pairs was identified around the optimal pair whose errors are within the 5% assay error variation. A larger region indicated poor identifiability and a smaller optimal region indicated more precise identifiability. Comparison of the two trials indicated if one method provides a more identifiable problem, and thus more precise results.

Result:
Trial B, without insulin boluses, has optimal parameter value regions 2.5x larger on average than trial A, with insulin boluses. The optimal parameter ranges between trials varies from 0.02 to 0.08 min^{-1} in general clearance, and 0.06 to 0.09 in first-pass clearance on average.

Conclusion:
Addition of an 1U exogenous insulin bolus improves the identifiability of hepatic clearance parameters. Adding a small intravenous insulin bolus in metabolic tests significantly improves identification and outcome test precision. Insulin assay errors require insulin modification of clinical tests to retain identifiability and precision.

Timed, and Timed-Insulin Dietary Glucose Disposal, (TGD(T,I) and TIGD(T,I), and Continuous Glucose Monitoring (CGM)

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Objective:
The objective is to refine carbohydrate counting (CC) and insulin administration using CGM and meal-related data to improve diabetic control, emphasizing the timing as well as the dosing of premeal insulin.

Method:
Two indices, TGD(T,I) and TIGD(T,I), were calculated utilizing CC with CGM meal-related time and the amount of insulin injected. T refers to $t_1 - t_0$, time between t injection of insulin and initial rise above baseline of ingested carbohydrate. I = amount of insulin injected at t_0. Interval from the rise and return to baseline of the glucose concentration curve = $t_3 - t_2$. TGD(T,I) = CC/t_3-t_2); TIGD(T,I) = CC/(t_3-t_2)*I. CC comes from personal diet and insulin recording and reference materials. Time intervals were obtained from the graphic CGM uploaded displays.

Result:
Example: Breakfast A equals Breakfast B: 6 strawberries, ½ cup uncooked oatmeal, ½ cup blueberries, ½ cup cottage cheese: 46 g glucose. Breakfast A = TGD (0,13) = 46000/(180) = 256 milligrams/minute; TIGD (0,13) = 46000/(180*13) = 19.7 mg/(min*unit) Breakfast B: TGD (45,12) = 46000/45 = 1022 mg/min; TIGD = 46000/(45*12) = 85.2 mg/(min*unit)

Conclusion:
These indices demonstrate the importance of the timing as well as the amount of insulin injected. Clearly similar amounts of insulin injected at various times prior to a meal have a markedly different impact on the height and the duration of the glucose concentration curve. Although the carbohydrate/insulin ratios were similar, glucose concentration curves were clearly impacted by injecting insulin further away from the glucose concentration rise. 15-20 minutes is usually chosen as a time optimizing insulin effect while reducing the risk of hypoglycemia. The TGD(T,I) and TIGD(T,I) clearly demonstrate that effect, adding another way of assessing CGM data..

Impact of BGM Point Profiles on Glycemic Variability Prediction Performances

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Objective:
Consistent measurements of the blood glucose levels in patients with diabetes are necessary in order to ensure the quality of the treatments administered. However, there is controversy over whether the emerging continuous glucose monitoring (CGM) devices are better than previous self-monitoring methods. This study investigates the effect that the number of blood glucose measurements taken per day has on a machine learning model's ability to accurately predict three variations for the next day: the mean blood glucose value, the occurrence of a hypoglycemic event, and the time-in-range percentage.

Method:
Blood glucose monitoring (BGM) data from Novo Nordisk clinical trials was used to assess the machine learning prediction performances of 1, 4, 7, and 9-point profiles (PP) in comparison to CGM data. Performance was measured by accuracy metric for classifier models and R-squared metric for regressor models. The machine learning models tested included support vector machine, gradient tree boosting, and random forest. Linear regression for regressor and logistic regression for classifier were used as baseline comparison models.

Result:
Mean blood glucose value: 1PP – 78.14%, 4PP – 45.07%, 7PP – 92.98%, 9PP – 98.96%. Hypoglycemia event: 1PP – 95%, 4PP – 69%, 7PP – 84%, 9PP – 99%. Time-in-range percentage: 1PP – N/A, 4PP – 16.40%, 7PP – 76.66%, 9PP – 98.62%.

Conclusion:
BGM data can perform equivalently to CGM data, with the most consistently accurate predictions corresponding to the 9PP. However, a 9PP is not the most viable option, since it would require patients to prick their fingers 8 times per day. Further analysis of the deficiencies and inaccuracies in lower point profiles is required in order to understand the optimal timings of the measurements and improve the performance as well as the overall patient experience.

Workplace Exposure to Environmental Pollution and Prevalence of Prediabetes and Type 2 Diabetes Mellitus

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Background:
Workplace exposure in various occupational and industrial sectors is an emerging health concern worldwide. This study aimed to investigate the workplace exposure for various occupational and industrial workers and prevalence of prediabetes and type 2 diabetes mellitus.

Method:
Initially, N=2500 male volunteers who were wood, welding, motor mechanic, and oil refinery workers were interviewed. After an examination of their demographics and medical history, N=1408 total workers: non-smoking wood (N=158), welding (N=560), motor mechanic (N=272), and oil refinery workers (N=217), along with N=201 control subjects, were selected. These workers had been exposed to their respective workplaces for 8 h per day, six days per week.

Result:
Subjects with an A1c of less than 5.7% were regarded as non-diabetics, A1c 5.7%-6.4% were considered prediabetics, and subjects with A1c more than 6.4% were considered diabetics. In wood industry workers, the prevalence of prediabetes (PD) was N=64 (40.50%), T2DM N=21 (13.29%); in welding workers, prediabetes was N=261 (46.60%), and T2DM was N=90 (16.07%); in motor mechanic workers, prediabetes was N=110 (40.44%), and T2DM was N=126 (46.32%); and in oil refinery workers, the prevalence of prediabetes was N=80 (36.86%), and T2DM was N=35 (16.12%). However; the combined prevalence of prediabetes and T2DM among wood, welding, motor mechanic, and oil refinery workers was N=421 (34.79%) and N=515 (42.66%), respectively.

Conclusion:
The prevalence of prediabetes and T2DM among various industrial workers increased with the duration of working exposure in the wood, welding, motor mechanic, and oil refinery industries. A one-year working exposure in these industries caused an increase of 0.03% in A1c.

SGLT2 Inhibitor Interference Testing with Accu-Chek® Blood Glucose Monitoring Systems

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Objective:
The objective of the study was to evaluate the performance of five Accu-Chek blood glucose monitoring systems in the presence of elevated concentrations of four SGLT2 inhibitors: canagliflozin (Invokana®), dapagliflozin (Farxiga®), empagliflozin (Jardiance®) and ertugliflozin (Steglatro®). SGLT2 inhibitors are commonly used in the treatment of type 2 diabetes and remove sugar from the body through the urine. The systems included in the study were Accu-Chek® Active, Accu-Chek® Aviva, Accu-Chek® Guide, Accu-Chek® Instant, and Accu-Chek® Performa.

Method:
A literature search was conducted to determine peak plasma concentrations of the four medications, and samples were prepared at five times the peak plasma concentrations of each medication. Test and control samples were prepared in whole blood at three glucose concentrations, and three strip lots were tested per system.

Result:
The samples were prepared per CLSI's *EP07 Interference Testing in Clinical Chemistry, 3rd edition*, and the substances were tested at the following target concentrations: canagliflozin (1.7 mg/dL), dapagliflozin (0.1 mg/dL), empagliflozin (0.3 mg/dL) and ertugliflozin (0.2 mg/dL). The bias between the test and control samples was calculated for each substance at each glucose level. The bias results were then evaluated against the acceptance criteria in ISO 15197:2013/EN ISO 15197:2015, which state that a substance is considered an interferent if the mean bias exceeds 10 mg/dL for glucose concentrations less than 100 mg/dL or exceeds 10% for glucose concentrations greater than or equal to 100 mg/dL. At the concentrations tested, canagliflozin, dapagliflozin, empagliflozin and ertugliflozin are not considered interfering substances with the Accu-Chek® systems in the study

Conclusion:
When using any of the four tested SGLT2 inhibitors, blood glucose results from the five tested Accu-Chek systems will not be biased.

Treatment Outcome Prediction of Type 2 Diabetes Patients on Once-Daily Basal Insulin Injection

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Objective:
The decision when to intensify the treatment from oral treatment to basal insulin is made by the health care professional for people with type 2 diabetes (T2D). In this context, treatment intensification relies heavily on the A1c test. Although several alternative oral treatments exist, basal insulin remains in general one of the most effective solutions for both treatment and cost for people with T2D. Hence, knowing at onset if basal treatment is the most suitable for treatment intensification for a patient is of high relevance. The aim of this study is to examine to what extent patient demographics and continuous glucose monitoring (CGM) data can enhance the ability to predict treatment outcome beyond what can be predicted based on A1c alone at treatment onset.

Method:
Clinical data were acquired from four different trials with a total of N=222 poorly regulated people with T2D (A1c ≥ 7%) on oral treatment initiating once-daily insulin injection. A1c, demographics, and expert-dependent CGM metrics (3 days) were available at onset. Logistic regression was used in a repeated stratified cross-validation setup to evaluate the performance predicting the binarized A1c value after 6 months defined as either acceptable (A1c < 7%) or poor (A1c ≥ 7%).

Result:
In all cases the performance exceeds the baseline (majority class) in terms of prediction accuracy. Adding demographics and CGM metrics as input to the models in the cross-validation setup improve treatment outcome predictions contrasted to using A1c alone at onset.

Conclusion:
The obtained results indicate improved performance when enhancing the input to the prediction models with demographics and CGM metrics in addition to A1c at onset. This points to demographics and CGM data being useful for the assessment of successful/unsuccessful treatment outcomes.

Predicting Success with a Diabetes mHealth Application from Early Usage Data

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Objective:
mHealth applications have the potential to improve glycemia and the overall health status of people with diabetes. However, some patients only minimally engage with these technologies and thus achieve suboptimal clinical outcomes. The goal of this study is to build a predictive model that, given early usage data from a diabetes mHealth application, can predict which patients will persist in using the application and/or experience improvement in blood glucose (BG).

Method:
A sample of N=238 type 2 diabetes patients were recruited via email to begin using a diabetes management mHealth application. The first 2 weeks of engagement data, as well as demographics, were collected and used as independent variables. Logistic discriminant analyses were run with consistent user persistence and a drop in either average or maximum BG as dependent variables. The BG value 14 mg/dL was used since it represents a change of approximately 0.5% A1C points.

Result:
Logistic discriminant analysis was able to predict users' consistent persistence at the month 3 and month 6 timepoints with 81.6% accuracy. A 14 mg/dL drop in either max or average BG at the month 3 and month 6 timepoints could be predicted with 79.8% accuracy.

Conclusion:
This study shows that it is possible to predict which users will consistently persist in using a diabetes mHealth application and/or experience an improvement in BG from just 2 weeks of initial usage data. Future research may potentially explain the factors affecting users likely to drop out or experience limited clinical improvement. Automated and early identification of patients unlikely to succeed in a mHealth protocol provides an opportunity to target these users with additional interventions to get them on track.

Significant Reduction in Time-Below-Range (Hypoglycemia) in People with Type 1 Diabetes using an Advanced Hybrid Closed Loop System

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Objective:
Hypoglycemia remains a significant concern around intensive glucose management for people with diabetes (PWD). Advanced hybrid closed-loop systems like Control-IQ technology can provide opportunities to assist PWDs better manage their time-below-range (TBR) or hypoglycemia while optimizing glycemic control.

Method:
This study was part of a larger project evaluating real world outcomes in early adopters of Control-IQ technology. We examined sensor TBR metrics for PWDs with type 1 diabetes (T1D) 30 days prior to starting Control-IQ technology (T1) and after 7 weeks of Control-IQ technology use (T2). Assessment of TBR metrics was guided by international guidelines i.e. <4% time/day with sensor reading (SR) <70mg/dL (Level 1) and <1% time/day with SR <54mg/dL (Level 2). Glycemic data was captured from the t:connect® web application. Wilcoxon-signed rank tests were performed to analyze change in median (IQR) TBR, and time-in-range (TIR) from T1 to T2.

Result: Of N=1127 participants at T1, N=232 PWDs were not meeting the TBR recommended guidelines. They were significantly more likely to be male, have longer diabetes duration, lower body weight, lower A1c, and better TIR compared to their counterparts who met TBR recommendations at T1 (n=895). For the N=232 PWDs, with Control-IQ technology use, significant reduction in TBR was noted at T2 for Level 1 (4.75% (2.94-6.66%) to 3.04% (1.63-4.62%)) and Level 2 hypoglycemia (0.86% (0.40-1.43%) to 0.54% (0.21-1.01%)), $p<0.001$. Overall, participants spent 24.6 minutes less/per day in Level 1 hypoglycemia and 4.6 minutes less/per day in Level 2 hypoglycemia at T2. Their TIR improved significantly from 76.95% (69.42-83.87%) (T1) to 83.74% (77.17-88.71%) (T2) ($p<0.001$).

Conclusion:
Control-IQ technology demonstrated a clinically relevant reduction in hypoglycemia with improved TIR in PWDs within a short period.

A New Model for Mealtime Insulin Dosing in Type 1 Diabetes: Retrospective Validation on CTR3 Dataset

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Objective:
Recently (Noaro et al., IEEE TBME, 2020), we proposed a new model for mealtime insulin dosing in type 1 diabetes (T1D) management based on least absolute shrinkage and selection operator (LASSO). We demonstrated, both *in silico* and using available clinical data, that the new model outperforms the current standard formula (SF) for insulin dosing used in common clinical practice. The aim of this work is to further validate the new LASSO model using a new independent dataset before moving onto ad hoc clinical trials.

Method:
Data collected during the CTR3 study (ClinicalTrials.gov ID: NCT02137512) were preprocessed by analyzing the 4-hour postprandial intervals where no corrective actions (e.g. hypotreatments or corrective boluses) were present. The selected data segments were divided into two different scenarios based on the glucose trend arrow (ΔG) at mealtime, i.e., increasing and decreasing ΔG (scenario A and B respectively). Then, to assess the efficacy of the LASSO model against SF, we applied ReplayBG, i.e., a newly proposed *in-silico* framework for the assessment of new therapy guidelines for T1D management using retrospective data.

Result:
Results in terms of percentage of time in the hyperglycemic, euglycemic, and hypoglycemic range were consistent with the results achieved in our paper, thus confirming the efficacy of our method. Specifically, compared to SF, we observed the improvement of the overall glycemic control in both scenario A and B when the LASSO model is adopted.

Conclusion:
In conclusion, the results obtained in this work confirm the positive impact of our new LASSO model for mealtime insulin dosing, thus supporting the setup of an ad hoc clinical trial for its validation in real life.

Development of the Modular Multi-Layer Microfluidic Chipset using the "Microfluidic Capillaries and Lymphatic" (MCAL) Chipset Design as the Proof of Concept for Future Development of the "mIslet" Chipset and its Compilation as Wearable and/or Implantable "mPancreas"

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Objective:
Utilizing the patented "MCAL" chipset design to prototype a biomimetically-designed multilayer-chipset for development of "mIslets" which have important features: 1)continuous blood perfusion 2)maintaining immunoisolation 3)providing nutrients and oxygen to satisfy the Islets' metabolic demands, and 4)allowing diffusion of insulin into the plasma. Compilation of "mIslet" biochipsets produces the wearable and implantable bioartificial pancreas-"mPancreas".

Method:
Chipsets were fabricated by sandwiching two PES-membranes (20kDa MW Cutoff) in between three microfluidic layers, creating a central layer to be used as an islet reservoir that provides immunoisolation. Blood perfusion via the outer layers allowed oxygen, glucose, nutrients and molecules [<20kDa such as insulin(MW-5.8kDa) and glucagon(MW-3.5kDa)] to diffuse to the blood based on patient's glucose level.

Result:
In experiments, anticoagulated bovine blood flowed through middle layer without cell damage, while serum-like fluid flowed through the two outer layers and significant diffusion of different size molecules (Creatinine, Phosphorus and Vitamin B12) occurred rapidly and continuously in between these three layers demonstrating that oxygen, glucose, insulin and glucagon can be exchanged if they are < 20kDa. This proof of concept would allow these 3D-structure chipsets to be populated with Islet that are perfused with blood providing the oxygen, nutrient, glucose, to the middle layer that contains islet or stem cells.

Conclusion:
We introduce a novel and biomimetically-designed three-layer microfluidic chipset with unique features providing continuous low blood flow to provide oxygen and nutrients through diffusion to the islets in an immunoisolated niche. These chipsets will be used to develop the "mIslet" chipsets to release insulin based on patient's glucose level emulating a pancreas. The compilation the "mIslets" will produce the wearable and/or implantable Bio-Artificial Pancreas termed "mPancreas" emulating true pancreas.

Use of Smartphones and Mobile Health Applications among Individual with Self-reported Diabetes Mellitus: Analysis of 2019 Health Information National Trends Survey

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Objective:
The purpose of this study was to examine the prevalence, acceptability, and potential for using digital health tools (smartphones and health apps) in health promotion for people with diabetes mellitus.

Method:
Data were pooled from cycle 3 (2019) of the 5th edition of the Health Information National Trends Survey (HINTS 5). Descriptive statistics were used to investigate the prevalence of smartphones and health apps ownership. The difference between health apps ownership versus non-ownership was examined among individuals with diabetes with regards to perceived usefulness of digital tools for managing their health, and intentions to adopt positive health behaviors using chi-squared tests. Multivariable logistic regression was used to identify sociodemographic predictors of health app ownership.

Result:
A total of N=1149 participants (21.7%) who self-reported diabetes mellitus was identified. The prevalence of digital health tools ownership was 77.7%, 53.8%, and 46.3% for smartphones, tablets, and mobile health apps respectively. Individuals with diabetes mellitus who had health apps installed on their devices were more likely to report intentions to lose weight than those without health apps. Further, they were also more likely to find these devices beneficial for health promotion. Of all the sociodemographic predictors, only the level of education significantly predicts health app ownership.

Conclusion:
Digital health tools have been accepted and are already being utilized by individuals with diabetes mellitus for self-care. In our study, the prevalence of health app ownership among those with diabetes is 46.3%. Education was an important predictor of health app ownership. This information is crucial and underscores the need to address potential barriers of mobile health adoption and ensure its broader applicability.

Use of Wearable Device among Adults in the US with Self-reported Diabetes Mellitus: An Analysis of the 2019 Health Information National Trends Survey

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Objective:
The objective of this study is to evaluate the prevalence, patterns, and sociodemographic predictors of wearable device use among individuals with self-reported diabetes mellitus.

Method:
Data for our analysis was drawn from cycle 3 (2019) of the 5th edition of the Health Information National Trends Survey (HINTS 5). Descriptive statistics were used to evaluate the demographic characteristics, prevalence, and frequency of wearable device use among individuals with diabetes mellitus. Multivariable logistic regression was used to identify the sociodemographic predictors of wearable device use.

Result:
We identified N=1149 individuals who self-reported diabetes mellitus. Of these, 51.2% were females, 59.3% were white, and 51.6% had less than a college education. The prevalence of wearable device use was 20%. Further, a large proportion (86.1%) of the wearable device users were willing to share information from their wearable devices with their healthcare provider, and almost half of them (43.4%) reported daily use of these devices in the past 1-month. Significant sociodemographic predictors of wearable device use include age, income, and level of education.

Conclusion:
Our results highlight the feasibility and acceptability of using wearable devices to deliver evidence-based health care to individuals with diabetes. Future interventions should consider the scalability of these tools and how to reach those subgroups of individuals with diabetes mellitus for whom current technologies may be unavailable.

Expected Variability in Estimated Insulin Secretion from C-peptide using Van Cauter Kinetic Parameters

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Objective:
Direct measurement of pancreatic insulin secretion is difficult from insulin assays alone, as inter-subject variability in hepatic extraction and peripheral clearance make it unidentifiable. C-peptide does not have the same physiological constraints and is commonly used to calculate insulin secretion using the well-known Van Cauter model. However, this model uses fixed relationships for three key model parameters, built from their study data, but containing significant variability. This study quantifies insulin secretion variation as a function of reported model parameter ranges.

Method:
Data was analyzed from N=39 healthy male subjects in a frequently-sampled intravenous glucose tolerance test (ivGTT). C-peptide values were used to calculate insulin secretion using Van Cauter's kinetic parameters. Monte Carlo analysis independently varied all three parameters within reported ranges, yielding N=10,000 combinations per subject (based on convergence analysis). Insulin secretion area under curve (AUC) represents total secreted insulin over first and second phase within the 40 minute test. Per-subject median AUC is what Van Cauter's model calculates. Normalizing each AUC by the participant's median value over all N=10,000 iterations quantified the expected model-based variability in AUC.

Result:
Median AUC was 5,741 mU and ranged from 2,761 mU – 13,858 mU across all subjects. Normalized per-subject, AUC ranged from 81% to 120% (25^{th}-75^{th} range) of the median value. Thus, Van Cauter modeled insulin secretion may vary by up to ±20% across all subjects from the standard model calculation. AUC total insulin variation was reflected in both first and second phase secretion.

Conclusion:
Kinetic parameters first proposed by Van Cauter may easily over or under-estimate insulin secretion from C-peptide measurements by ±20%. This variability will impact outcome insulin kinetic parameters and secretion based diagnostics.

Adoption of CDISC Clinical Data Standards for Type 1 Diabetes (T1D) Device Data

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Objective:
Creation and adoption of clinical data standards that support diabetes technology data will transform incompatible and disparate data into universal and illuminating information, facilitating discoveries that could have invaluable impact on T1D clinical research. Implementation of CDISC standards allow collection, organization, and analysis of data in a clear and consistent manner allowing *all* researchers to leverage information from studies globally.

Method:
With support from The Leona M. and Harry B. Helmsley Charitable Trust, CDISC is leading a unique, consensus-driven effort, bringing together T1D experts from academia and industry, to build on existing CDISC diabetes standards to create T1D clinical data standards in pediatrics, devices, exercise, nutrition and screening, staging, and monitoring of pre-clinical T1D.

Result:
In September 2020, pediatrics and devices standards are published at https://www.cdisc.org/standards/therapeutic-areas and freely available. Data models and standard formats have been developed that can represent the following:
- Identification of all devices and components for management of T1D
- Device properties and settings
- Participant utilization of devices
- Device events and user experience (e.g., DKA, Hypoglycemia etc.)
- Diabetes History
- Vital Signs and Growth Percentiles
- Pubertal Status

Additional standards related to T1D are due for publication towards the end of 2020.

Conclusion:
To make the greatest impact on T1D research, widespread promotion of the availability of standards for researchers to adopt and implement is of highest importance. CDISC provides complementary education courses and implementation information to assist in this adoption. Widespread adoption of the standards will bring clarity to T1D data and will enable the accessibility, interoperability, and reusability of data, driving operational efficiencies, expediting regulatory review, and reducing time to market.

Telehealth: Keeping Young People with Type 1 Diabetes Mellitus Connected to Healthcare during the COVID-19 Pandemic

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Objective:
To examine the experiences of young people with type 1 diabetes mellitus (T1DM) in accessing healthcare during the COVID-19 pandemic in Australia.

Method:
A qualitative methodological approach was used involving semi-structured interviews (n=11) and thematic analysis. A purposive sample of young people aged 12-16 years with T1DM (accompanied by a parent) were interviewed via Zoom or telephone between June and July 2020. Interviews lasted 20-40 minutes and were recorded and transcribed.

Result:
Three key themes were identified: feeling vulnerable; new ways of accessing care; and feeling well-supported by the healthcare team. Participants were aware that T1DM made them more vulnerable to poor outcomes if they contracted COVID-19. In some cases, due to this, usual face-to-face care was postponed or not sought. Participants relied on three-monthly appointments with the diabetes healthcare team to review and plan their diabetes management. Telehealth consultations offered a convenient and contactless way to continue this. The greatest differences were not having access to the whole team at one appointment (endocrinologist, dietitian, diabetes educator, psychologist), or to physical examination and A1c testing during telehealth consultations. However, participants were secure in the knowledge that they could contact team members via email or telephone for advice and trusted their team to advise them if a face-to-face consultation was necessary. Some felt a video option might be better than telephone. Most participants considered using telehealth for some, but not all, consultations with the diabetes health service as part of their future healthcare routine.

Conclusion:
Telehealth consultations offer convenient, safe, and contactless access to healthcare professionals during COVID-19. The added value of video consultations and whole team access need to be considered for future clinical implementation of telehealth.

Pulsatile Insulin Treatment as a Treatment Option for Patients with Type 2 Diabetes and Stage III Kidney Failure – Results from a Pilot Study

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Introduction:
In healthy individuals, insulin is secreted by the pancreatic ß-cells in a pulsatile fashion with about 10-12 pulses/hour. Loss of this pulsatility is one of the first indications of ß-cell dysfunction leading to type 2 diabetes. This pulsatility of insulin secretion is considered a trigger mechanism for the regulation of hepatic gluconeogenesis and for maintaining the sensitivity of peripheral metabolic and vascular insulin receptors. Various attempts have been made over the last 30 years to use pulsatile intravenous (iv) insulin infusion therapy (PIT) for treatment of diabetes and secondary complications. The purpose of this prospective, randomized pilot study was to investigate the effect of once weekly PIT (2 h vs. 3 h procedures) over a period of 3 months on parameters of kidney function in patients with type 2 diabetes and chronic renal failure (glomerular filtration rate (GFR) < 60 mL/min).

Method:
Of the N=22 enrolled type 2 patients, N=17 performed the trial per protocol (7 women, 10 men, age: 69±7 yrs., A1c: 7.9±1.0 %). They received a total of 10 PIT procedures (2h: 9 patients/3h:8 patients). Observation parameters measured at baseline and endpoint were A1c, glomerular filtration rate (GFR) using the MDRD formula, body weight, blood pressure, creatinine, nerve perception thresholds (pain, warm, cold, vibration, assessed by path tester), and treatment satisfaction (DTSQ).

Result:
At endpoint, there were no significant differences between the two groups, and the final results are presented for the whole population. GFR improved by 12 % (from 47.6±10.0 mL/min to 53.3±11.9 mL/min, $p<0.01$) and creatinine decreased by 7 % (1.43±0.29 mg/dL vs. 1.33±0.34 mg/dL, $p<0.05$). Stable results were seen for A1c (-0.1%), body weight (-0.5 kg) and blood pressure (systolic/diastolic: -4%/0%, all n.s.). No changes were seen in nerve perception thresholds for any of the investigated sensory fiber qualities. The sum score for treatment satisfaction improved from 3.6±2.3 to 2.9±2.1 at endpoint ($p<0.05$). The treatments were well-tolerated; however, 8 treatment-related events of muscle cramps were reported for N=5 patients during the PIT procedures.

Conclusion:
In conclusion, an improvement in kidney function and treatment satisfaction was observed after 3 months of PIT in patients with type 2 diabetes and renal failure, irrespective of the duration of the procedure (2h vs. 3h). The results of this pilot trial will now be used to design an appropriate confirmatory study to investigate the effect of PIT when given in addition to standard of care treatment vs. standard of care alone.

Use of the Sencell Osmotic Pressure-Based Glucose Sensor in a Standard Needle Sensor Environment

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Introduction:
The size of the measurement chamber of the injectable Sencell Glucose Sensor (Lifecare, Norway) is smaller than 0.7 x 0.35 x 0.7 mm^3. It uses an active fluid with a glucose binding molecule (GBM) and a glucose-like ligand to transfer external glucose concentrations into measurable osmotic pressure signals. The reversible affinity reaction in the chamber does not consume any molecule when generating the signal, resulting in a potential for long-term survival of the sensor in the body. The small size of the sensing element allows also for integration into a standard needle sensor environment.

Method:
The miniaturization of the sensor without losing pressure sensing sensitivity was achieved by a proprietary, nanosensor technology. Micro-electromechanical systems (MEMS) fabrication techniques were used to build a sensor chamber with less than 1 mm^3 volume and the pressure membrane was equipped with nano-strain sensor (4 x 1 μm^2). For preparation of needle sensor prototypes, the chamber was embedded into a steel needle and connected by wire to an electronic read-out interface. Sensor calibration was performed over a broad dynamic glucose concentration range. The observed sensor specifications (pressure range: <-300 to >300 mbar, pressure resolution 480 µbar, membrane size 1x1mm^2, 300 nm thickness) should allow it to track glucose changes with a resolution of 1-2 mg/dL.

Result:
The collected signals showed a very sensitive and linear pressure to signal relation (r^2=0.996), a high reproducibility (CV = 0.2 %), no hysteresis/drift over time, and a high stability even when performing continuous repetitive calibration procedures.

Conclusion:
In conclusion, needle sensor prototypes based on the core Sencell sensor technology have been developed, which could be potentially integrated into existing needle sensor products. This could enhance longevity and accuracy by providing orthogonal glucose signals, which could be used for cross-calibration. Clinical studies with the prototypes to test the *in-vivo* performance of the technology have been initiated.

Insulin Pump Therapy Is Useful for Type 1 Diabetes Regardless of Variable Demographics

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Objective:
Insulin pump therapy has demonstrated benefits in terms of glycemic optimization and patient satisfaction. However, despite being a technologically advanced insulin delivery system it requires substantial input from its users to work optimally. This can be influenced by several demographic variables of the user population. This study aims to evaluate the demographic data of patients using insulin pump therapy in relation to improvement in glycemic control

Method:
This retrospective observational study included all patients with type 1 diabetes who attended the insulin pump clinic in two hospitals in the Aneurin Bevan health board, South Wales in 2019. Statistical analysis was performed using SPSS.

Result:
N=108 patients were included in the study with a mean age of 41.25 years (SD 14.547 years). The mean pre-pump A1c was 66.08 mmol/mol (SD 14.32 mmol/mol). In total, N=97 patients had an A1c 6-months post-pump initiation (mean 60.26 mmol/mol); N=66 patients 12-months post (mean 60.17 mmol/mol) and N=56 patients 18-months (mean 60.64 mmol/mol). In total 31/108 (28.7%) patients had previous experience with a pump.

Conclusion:
This study demonstrated trends towards an improvement in A1c that was sustained at 18-months. These trends were observed in patients regardless of their hospital site, previous experience with pump therapy, or age. Larger studies are required to confirm these results but our work supports pump therapy being offered to a wide demographic population, as benefits were seen throughout.

Clinical Relevance of Reapplication of Blood Samples During Blood Glucose Testing

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Objective:
Second-Chance™ Sampling (SCS) is a feature of some BGMSs that allows users to apply more blood to the test strip if the first attempt had insufficient volume, reducing the need to re-lance. Utilization of SCS has not been examined outside of a registrational trial setting. This analysis utilizes CONTOUR®DIABETES app (CDA) cloud data and examines the use of SCS and if there are differences between patient groups based on patient reported data. Additionally, the data were assessed if SCS was used more when blood glucose values were above or below 70 mg/dL.

Method:
A retrospective observational analysis was performed on worldwide CDA users in February 2020. ANOVA was performed on SCS users for several variables including diabetes type, therapy, age and gender. Additionally odds ratios were calculated to assess whether the probability of using SCS was greater when blood glucose values were above or below 70 mg/dL.

Result:
Significant differences in percent of SCS use were observed for diabetes type ($P=0.0019$), age ($P<0.0001$), gender ($P< 0.0001$) and therapy profile ($P=0.0019$). SCS use was more likely when blood glucose was below 70 mg/dL than above 70 mg/dL (OR 1.4, 95% CI 0.9965, 1.8318).

Conclusion:
Utilization of SCS differs depending on diabetes type, gender, age and therapy. SCS can reduce the need to re-lance and prevent the waste of up to 12.68% of test strips in specific patient groups. Therefore BGMS's with SCS feature should be considered particularly for patients who use SCS the most.

Glycemic Outcomes with Adjustable Settings in the Advanced Hybrid Closed-loop (AHCL) System-Pivotal Trial

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Objective:
The MiniMed™ AHCL algorithm has several important advances over the MiniMed™ 670G algorithm including upgraded safety features, two user-adjustable basal target (BT) setpoints, and an automated correction bolus feature (the aggressiveness of which can be adjusted by changing active insulin time [AIT]). We evaluated the effects of various BT and AIT settings on glycemic outcomes.

Method:
A post-hoc analysis of data from a multi-center, single-arm pivotal trial (N=157 participants with T1D, 14–75 years) that had a ~2-week baseline period and a 90-day study period (AHCL algorithm engaged) was conducted. At ~45 days into the study period, participants switched BT from 100 to 120mg/dL, or vice-versa. The impact of BT and AIT on percentage of time spent below range (TBR<70mg/dL) and within range (TIR70-180mg/dL) was assessed.

Result:
Data were stratified by BT and further divided into four groups based on AIT (2, >2–3, >3–4, and >4 hours). To be included in the analysis, 14 consecutive days of SG-data were required after a BT and/or AIT change. There were 12 cases with the most aggressive settings (100mg/dL BT and 2-hour AIT) where the average(SD) of TIR and TBR were 78.5%(7.1%) and 2.9%(2.0%), respectively. Conversely, 33 cases were identified with the least aggressive settings (120mg/dL BT and >4-hour AIT) where similar metrics were 71.6%(6.6%) and 1.1%(0.8%), respectively. There were no episodes of severe hypoglycemia or DKA in any group.

Conclusion:
The data show that the AHCL algorithm is safe and effective across the spectrum of BT/AIT settings studied. The TIR increased by 6.9% with a slightly increased TBR that remained below 4%, at the most aggressive setting, indicating flexible user-adjustable settings that safely optimize glycemic control.

Diabetes Mobile Apps and COVID-19

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Objective:
Do diabetes apps contain accessible information about COVID-19 and its symptoms?

Method:
Using the search term "diabetes," the top ten most downloaded android and iOS apps were assessed in the Google Play Store/Apple App Store, respectively. Inclusion criteria: 1) Android: Downloads > 100,000; iOS: Reviews > 300 2) Free 3) Ability to track health data: A1C and FBS. Language Accessibility: Checked for in-app language settings; if none, changed language setting on device.

Result:
In the Play Store, the top ten apps in descending order were: 1) mySugr, 2) Onetouch Reveal, 3) OneDrop Diabetes Management, 4) Diabetes: M, 5) Health2Sync - Diabetes Care, 6) Diabetes, 7) Ontrack Diabetes, 8) Blood Glucose Tracker, 9) Glucose Buddy Diabetes Tracker, and 10) Diabetes Connect. In the App Store, the top ten apps in descending order were: 1) OneTouch Reveal, 2) Glucose Buddy Diabetes, 3) One Drop for Diabetes, 4) Glucose - Blood Sugar Tracker, 5) Blood Sugar Monitor by Dario, 6) mySugr, 7) Sugarmate, 8) DiabetesPal, 9) Diabetes:M, 10) Center Health - The Diabetes App. Of the ten Android apps: 0/10 had COVID symptom information in the app; 3/10 had a COVID statement; In-app language settings: 2/10 had Spanish and 1/10 had Chinese; After changing device language settings: 4/10 had Spanish and 1/10 had Chinese. Of the ten iOS apps: 0/10 had COVID symptom information in the app; 4/10 had a COVID statement (Only mySugr has CDC link for COVID information); In-app language settings: 1/10 had Spanish and 0/10 had Chinese settings; after changing device language settings: 5/10 had Spanish; 3/10 had Chinese.

Conclusion:
Of the top 20 diabetes apps, none of them had any information about COVID and its symptoms in the app. Also, the overall language accessibility is limited.

Classification of Daily Continuous Glucose Monitoring (CGM) Profiles in Type 1 Diabetes Using Layered Clustering and Clinical Metrics

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Objective:
The objective of this study is to propose a new methodology classifying CGM profiles into a limited number of distinguishable classes with unique clinical characteristics in order to assist with the interpretation of CGM data.

Method:
CGM daily profiles were derived from two clinical studies of the International Diabetes Closed-loop Trial, DCLP1 and DCLP3, recruiting N=127 and N=168 patients with T1D, respectively. Each 24-hour midnight-to-midnight CGM profile was partitioned into 8-hour non-overlapping intervals, clustered in a layered manner using K-means based on mean CGM (high vs low) and variability (high vs low Hourly Risk Range) to generate 64 clusters. Cluster centroids were determined from DCLP1 data (training set) and then used to classify the CGM profiles of DCLP3 (testing set).

Result:
Good cluster separation was observed in DCLP1 (mean cluster overlap of 34±16%) and confirmed by DCLP3 (mean overlap 37±18%). The classifier robustness was further confirmed by showing that corresponding clusters originating from the training and testing sets had similar shape (overlap 77±10%). In line with previously reported clinical outcomes (*NEJM*, October 2019), the classifier distinguished well DCLP3 patients on closed-loop control (CLC, N=112) vs. those on sensor-augmented pump (SAP, N=56), with 44% of profiles on CLC vs 36% of profiles on SAP classified in the clusters with lowest variability.

Conclusion:
A novel method for classification of daily CGM profiles generated a limited number of classes distinguishable by their shape and clinical characteristics. The methodology can distinguish between different treatment modalities and can be used to enhance the performance of decision support or closed-loop systems.

Impact of the MiniMed™ AHCL System on Post-prandial Glucose after a Missed Meal Bolus in Adolescents and Adults with Type 1 Diabetes (T1D)

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Objective:
Missed meal boluses are not uncommon and often result in hyperglycemia. This exploratory study assessed effects of the MiniMed™ AHCL system that autocorrects to 120mg/dL every 5 minutes on sensor glucose (SG) after a missed meal bolus, during the system pivotal trial in individuals with T1D.

Method:
Pre-prandial and post-prandial data from N=18 adolescents (14-21yrs) and N=66 adults (22-75yrs) were compared after a missed bolus for a dinner meal (±30% carbohydrate difference) on one day during a 2-week run-in and 90-day study phase (at basal target [BT] 100mg/dL). Differences in SG, time spent above range (TAR>180mg/dL and TAR>250mg/dL), within range (TIR70-180mgd/dL), and other metrics between run-in and study were determined.

Result:
Study phase Auto Bolus initiation reduced post-prandial SG after a missed meal bolus by 49.3% and 58.0% at 0-2hrs and 0-4hrs post-meal, respectively, for adolescents; and by 17.8% and 30.5%, respectively, for adults. Peak SG was reduced by 49.8% and 52.6%, respectively, for adolescents; and by 24.3% and 29.6%, respectively, for adults. In adolescents, the meal-induced increase in TAR>180mg/dL was lowered by 56.9% and 54.2%, respectively; and that in TAR>250mg/dL by 52.0% and 65.4%, respectively. In adults, the increased TAR>180mg/dL and TAR>250mg/dL were lowered by 20.2% and 36.3%, respectively; and by 35.3% and 47.5%, respectively. At each post-meal period, adolescent and adult post-prandial TIR improved by 50.9% and 49.1% and by 35.5% and 45.2%, respectively, compared to run-in. The run-in and study post-prandial TBR for each group was reduced.

Conclusion:
The AHCL system (at BT 100 mg/dL) helps to reduce hyperglycemia after a missed dinner meal bolus in adults and adolescents, the latter in whom glucose control is known to be difficult.

Accuracy Assessment of the New GlucoMen® Day CGM System in Individuals with Type 1 Diabetes

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Objective
The GlucoMen® Day CGM (WaveForm® Cascade) is a state-of-the-art continuous glucose monitoring (CGM) system designed for needle-free insertion that delivers one glucose reading every minute for up to 14 days [recently launched by A. Menarini Diagnostics (Italy)]. The objective of the present study is to assess the GlucoMen® Day CGM system accuracy against a laboratory reference instrument.

Method
Eight individuals with type 1 diabetes (N=3 female, mean age: 41.6 ± 13.3 years, BMI 28.0 ± 6.1 kg/m^2, A1c 55.6 ± 12.2 mmol/mol, diabetes duration 13.9 ± 6.5 years) used the GlucoMen® Day CGM system under routine conditions for a period of two weeks. Each subject had two CGM systems inserted simultaneously into the subcutaneous tissue of the abdomen where they remained for the full fourteen days. On days four and ten, a 5-hour meal/insulin challenge test was performed at the clinic to assess the CGM system performance during rapid glucose excursions. The serum glucose concentration was determined at the bedside in 20-minute intervals with a glucose oxidase reference method (YSI 2300 Stat Plus). The GlucoMen® Day CGM system accuracy was assessed by calculating the overall median absolute relative difference (MARD) and the mean absolute difference (MAD), and by performing the Consensus Error Grid analysis.

Result
The MARD and the MAD calculated for the two days spent at the clinic were 9.7 (2.6-14.6)% and 20.5 (9.5-24.0) mg/dL, respectively. The Consensus Error Grid analysis showed that 98% of data points were in the clinically acceptable zones A and B.

Conclusion
The study data indicate that in terms of accuracy the GlucoMen® Day CGM system meets the current clinical requirements for the state-of-the-art continuous glucose monitors.

Differences in Perceived Quality of Sleep and Satisfaction with Insulin Delivery Device in People with Diabetes

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Objective:
Poor sleep quality can impair glycemic control in people with diabetes (PwD). It is important to understand factors affecting sleep-related outcomes in PwD. However, we know little about sleep-related implications of new-age diabetes management devices.

Method:
PwDs from a diabetes research company's 2019 US-based panel were invited to participate in this IRB-exempt study. Participants with type 1 (T1D) or type 2 diabetes using insulin completed surveys including items on perceived quality of sleep (QoS) and satisfaction with their insulin delivery device (IDD).

Result:
Sample included n=763 PwDs [88% Caucasian, 71% T1D, 64% female, mean age = 51.95 (SD=17.37), mean diabetes duration = 24.53 years (SD=14.7)]. For IDD, participants were using multiple daily injection (MDI, n=394), patch pump (Omnipod® System, n=155), predictive low glucose suspend system (PLGS) (t:slim X2™ Pump with Basal-IQ™ technology, n=117) or hybrid closed-loop system (HCL) (MiniMed™ 670G System, n=97). Analysis of variance demonstrated differences in QoS across IDDs, with PLGS users reporting higher perceived QoS (mean=8.93, SD=1.69) vs. other IDD users ($p<.001$). MDI users reported the lowest perceived QoS (mean=6.81, SD=2.42). PLGS users reported higher IDD-related satisfaction (mean=8.84, SD=1.17) compared to other participants ($p<.001$). HCL users reported the lowest satisfaction (mean=7.53, SD=1.94). Multiple regression revealed perceived QoS as a significant predictor of IDD-related satisfaction ($\beta=.13$, $p<.001$). Qualitative analysis of open-ended questions on IDD-related satisfaction and trust highlighted other features valued by participants, including convenient software updates, user-friendly data uploads, and ability to use the device discreetly.

Conclusion:
Results demonstrate a notable relationship between IDD type and QoS. Discussion around sleep-related implications of IDDs with PwDs is recommended, as these may have an impact on their long-term use and overall diabetes management.

Smart Insulin Pens Allows Correction Doses as Needed Without Compromising Time Below Range

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Objective:
Smart Insulin Pen (SIP) features allow opportunities to safely deliver more frequent rapid-acting insulin doses. Previous research shows that as the number of rapid-acting injections per day increases, Time in Range (TIR) improves while maintaining clinical recommendations for Time Below Range (TBR). The purpose of this research is to describe the dosing behaviors of SIP users who inject more frequently and their likelihood to deliver correction-only doses when needed between meals.

Method:
Real-world clinical data from pediatric and adult SIP users (InPen, Companion Medical) were used to determine the frequency of delivering correction-only doses. Users included in the analysis required at least 60 days of paired InPen and continuous glucose data available from January through August of 2020. Users were categorized into six groups based on the average number of injections per day (>/= 1 through >/= 6). The frequency of users delivering correction only doses (vs. doses with meals) was compared across groups.

Result:
An analysis of N=2,816 users demonstrated a significant increase in the frequency of delivering correction-only doses by users who dose more per day (43% for users with ≥6 doses/day) compared to those who dose less frequently (28-33% for users with 1 to ≤ 4 doses/day), while maintaining TBR within clinical guidelines (2.8%).

Conclusion:
These findings suggest that users who dose more frequently are more likely to correct high glucose values between meals. This research supports the use of SIPs to challenge the multiple daily injection (MDI) clinical paradigm of only dosing at mealtime to avoid the risk of insulin stacking and hypoglycemia.

Preliminary Assessment of a Mass Manufacturable Point-of-Care Insulin Sensor

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Objective:
Measurement of circulating insulin levels is a promising method for improving glycemic management for patients with diabetes by allowing determination of individual insulin-glucose dose response relationships. Co-monitoring of insulin and glucose could reduce a patient's chances of hypoglycemia and enhance dosing control. Clinical immunoassays are available for insulin but require expensive equipment, and there is currently no insulin monitoring device on the consumer market. We propose a mass manufacturable point-of-care (POC), electrochemical sensor to rapidly measure blood insulin concentration, giving patients and clinicians a more accurate way to determine proper insulin dosing when combined with glucose monitoring. Work conducted will aim to verify the reproducibility of the POC platform, using purified samples, along with laying the groundwork for continuous sensing.

Method:
Sensors were prepared by immobilizing a self-assembling monolayer onto a gold screen printed electrode followed by attaching a monoclonal insulin antibody. Using electrochemical impedance spectroscopy and a $(Fe(CN)_6)^{3-}$ redox probe, a calibration curve was generated over the range of 0-2000 pM and validated with ELISA.

Result:
The imaginary impedance response of the antibody based, gold screen printed calibration curve has an R-squared of 0.95 with a slope of 21.4 mOhm/(pM) and an optimal frequency of 3125 Hz. Sensors have been tested to be under 15% coefficient of variance on benchtop studies with purified insulin solution.

Conclusion:
Current results support the feasibility of a development of POC insulin sensor. The sensor's application towards continuous sensing needs to be further developed due to insulin antibody high binding affinity. Future work will involve attaching an insulin aptamer for continuous detection and an animal study to validate the POC & continuous sensors.

Diabetes Information and Communications Technologies for Teens and Schools

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Objective:
Giving teens the ability to understand and optimally manage their type 1 diabetes mellitus (T1DM) will improve the quality of their school experience while improving their long-term health outcomes. This ongoing project co-designs, co-develops, and co-evaluates personalized user-focused *information and communications technologies* (ICTs) to enhance co- and self-management of T1DM for teenagers in the education setting.

Method:
We are collaborating with 12–17-year-olds, carers, and school representatives in the home and school environment to develop an ICT platform to support safe management of T1DM in schools that meets adolescents' needs and preferences, attracts long term use through "stickiness", and is a valuable source of diabetes management knowledge for school-based carers.

Result:
Our initial experiments have enabled the development of proof-of-concept, consumer-friendly, communication and information sharing tools for T1DM management. This involves an individualized online Diabetes School Management Plan, linked to a mobile App and web search engine, to help young people and schools to optimally manage diabetes. User study findings are informing the creation of "hypothetical" scenarios, which could derail self-management, and realistic-yet-synthetic annotated resources for ICT development and evaluation. These resources will enable us to challenge software developers, researchers, and students to submit solutions to a hackathon in 2020–2021, which will be evaluated by teenagers, their carers, and health professionals.

Conclusion:
Our outcomes will inform the next stage of developing ICTs for teens and schools. These, in turn, will enable better management of T1DM in education environments, improving the quality of life of affected adolescents, and reduced disease-associated psychomorbidity and long-term complications of their disease.

Insulin, Not the Preservative *m*-Cresol, Instigates Loss of Infusion Site Patency Over Extended Durations of CSII in Diabetic Swine

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Objective:
Insulin infusion sets worn for greater than 4-5 days have been associated with a greater risk of unexplained hyperglycemia. We examined the role of the preservative *m*-cresol in inflammation and changes in infusion site patency when infusion sets are worn for extended periods of time in a diabetic swine model.

Method:
In this cross-over study, insulin pharmacokinetics (PK) and glucose pharmacodynamics (PD) were measured on delivery of a bolus of regular human insulin U-100, formulated either with or without 2.5 mg/mL *m*-cresol, in N=17 fasted diabetic swine, following 0, 3, 5, 7, and 10 days of continuous subcutaneous insulin infusion (CSII). In a subsequent study in the same animals, biopsies were collected and evaluated from swine wearing infusion sets infusing (a) nothing, (b) saline, (c) regular human insulin U-100 with 2.5 mg/mL *m*-cresol, or (d) regular human insulin U-100 with no *m*-cresol, following 3, 7, and 10 days of CSII.

Result:
Exposure to *m*-cresol did not result in a statistically significant impact to any PK or PD endpoints. PK and PD responses dropped markedly from Day 7 to Day 10, regardless of the presence of *m*-cresol. Histopathology results suggest an additive inflammatory response to both the infusion set and the insulin protein itself, with inflammation peaking at Day 7 and remaining stable beyond, and no discernable effect due to the preservative.

Conclusion:
The preservative *m*-cresol was not found to contribute to either inflammation or changes in PK/PD endpoints over the course of 10 days of CSII. Rather, the insulin protein itself was observed to instigate a heightened and prolonged inflammatory response.

Long-Term Virtual Health Coaching as an Accessible and Impactful Tool for Diabetes Management

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Objective:
Virtual health coaching platforms, in which care teams provide remote monitoring or guidance, are an increasingly popular means of supporting patients between healthcare provider visits. This study investigated the potential for health coaching apps to address barriers to diabetes management and improve patient-reported health outcomes.

Method:
N=4,962 type 1 and type 2 diabetes patients from an opted-in US research panel were surveyed. A total of N=126 respondents currently use virtual health coaching apps, and another N=211 have used them in the past.

Result:
Patients who use health coaching apps are more likely to face barriers to diabetes management like lack of access to diabetes specialists (14%) and lack of insurance coverage for preferred therapies (27%), compared to those using health apps without coaching (6%, 16%), or not using health apps (8%, 15%). Those who used health coaching apps for over one year are more likely to report decreased A1c (59%) compared to those who used health coaching apps for 3-12 months (27%) and 3 months or less (13%). Those with a tenure of 3-12 months were more likely to report increased exercise levels (51%) and less likely to experience no benefits (16%), compared to those with a tenure of 3 months or less (20%, 38%). Of the patients who explained why they stopped using health coaching apps, 11% report cost-related reasons, while 19% found the programs too time-consuming.

Conclusion:
Patients receiving virtual health coaching are less likely to have access to healthcare and support in their diabetes management. As long-term health coaching app usage is associated with improved health outcomes, increasing access to virtual health coaching may be beneficial for populations facing barriers to care.

Intravenous Automated Blood Glucose Control with No Meal Announcement. A Prospective Time-in-Range *in silico* Study

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Objective:
We have developed an innovative blood glucose control technology based on intravenous (IV) blood sampling and delivery of insulin. Compared to current subcutaneous technologies, the IV pathway enables more accurate measurements and faster insulin effect. In this work, we present the effect of the IV pathway, combined with a PID controller, on maintaining the glucose level within the narrow glycemic range (70-140 mg/dl) for type 1 diabetes *in silico* subjects. Given the reduced delays, no prior meal or activity information is required.

Method:
The simulations were performed on two *in silico* type 1 diabetes subject models: the UVa/Padova T1DMS model (N=33 subjects) and the NudgeBG model (N=1000 subjects, including the effect of unmeasured sources of variation such as stress and exercise). For each subject, glucose profiles were simulated for two days involving four meals/day (three main meals and a late-evening snack; 20-70 grams of carbohydrates/meal). Measurement and insulin delivery errors were included in the simulation. The control interval was 15 minutes.

Result:
UVa/Padova T1DMS model - blood glucose median: 115.40 mg/dl (Q_{25}=108.78, Q_{75}=124.93); time in the 70-140 mg/dl range: 87.71%; time in the 70-180 mg/dl range: 97.03%; time below 70 mg/dl: 0.85%;time above 140 mg/dl: 11.42%.
NudgeBG model - blood glucose median: 118.40 mg/dl (Q_{25}=110.96, Q_{75}=129.62); time in the 70-140 mg/dl range: 81.54%; time in the 70-180 mg/dl range: 93.31%; time below 70 mg/dl: 0.33%; time above 140 mg/dl: 18.12%.

Conclusion:
The simulations show that IV blood sampling for glucose measurement and IV insulin delivery, combined with a closed-loop PID controller, provide effective blood glucose management. It provides high time in range and reduced hypoglycemia risk, without requiring meal or physical activity announcement.

Regional COVID-19 Disease Burden and Individual Changes in Glycemic Control

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Objective:
Morbidity and mortality caused by COVID-19 are unevenly distributed. We sought to correlate county-specific COVID-19 mortality with changes in a CGM-based metric of glycemic control.

Method:
Data were from a convenience sample of US-based users of the G6 CGM System (Dexcom, Inc., San Diego, CA) with known residential postal codes. Users resided in counties having at least 1 death attributed to COVID-19 as of May 21 and included at least N=200 G6 users. In addition, users had to have uploaded ≥200 glucose values/day for ≥8 weeks in the pre-pandemic and intra-pandemic intervals (defined as the eight weeks ending on 3/1/2020 and 6/14/2020, respectively). County-level COVID-19 mortality figures as of May 21, 2020 were aggregated by and obtained from the New York Times. Time in range (TIR) was the percentage of glucose values in the 70-180 mg/dL range. Within each county, the proportion of individuals who experienced a TIR increase of at least 5 percentage points between pre-pandemic and intra-pandemic intervals was calculated.

Result:
A total of N=35,274 G6 users from 100 counties or county-equivalents provided data. The highest mortality was 20,491 in the five counties comprising New York City. The proportion of G6 users experiencing at least a 5% improvement in TIR ranged from 24.8% (Douglas, Nebraska) to 42.0% (Wayne, Michigan). This proportion and the logarithm of COVID-19 mortality were positively correlated ($r=0.40$, $p<0.001$); counties with more COVID-19 deaths tended to have more patients with clinically meaningful improvements in TIR.

Conclusion:
The local burden imposed by the COVID-19 pandemic may be associated with local changes in behaviors or diabetes management strategies that improve the adequacy of glycemic control.

Variations in Time in Range Assessed by CGM in the Early COVID-19 Pandemic

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Objective:
Global disruptions in the early months of the COVID-19 pandemic are reflected in changes to diabetes management strategies among users of continuous glucose monitoring (CGM) systems. We examined time in range (TIR) before and during the pandemic in areas with different median incomes.

Method:
Pre-pandemic and intra-pandemic observation windows were defined as the four weeks ending on February 16 and May 17, 2020, respectively. TIR was defined as the percentage of sensor glucose values in the 70-180 mg/dL range. Data were from US-based users of the Dexcom G6 CGM system (Dexcom, Inc., San Diego, CA) with known ZIP codes who had uploaded data on or before January 1, 2020, who had uploaded ≥1 value/month in the first 5 months of 2020, and who had uploaded ≥200 values/day for ≥4 days/week in both the pre-pandemic and intra-pandemic observation windows. Groups of ZIP codes were established based on 2018 estimates of median household income (bins ranging from <$50,000 to ≥$150,000), poverty rates (bins ranging from <5% to ≥30.1%), and Gini index (a measure of income inequality; bins ranging from <0.4 to >0.5).

Result:
TIR improved from the pre-pandemic to the intra-pandemic observation window regardless of median income level, poverty rate, or Gini index. Intra-pandemic TIR in areas with the lowest median income, highest poverty, and lowest income inequality were significantly lower than pre-pandemic TIR in areas with the highest income, lowest poverty, and highest income inequality.

Conclusion:
Although the early months of the COVID-19 pandemic were associated with improved TIR, the magnitude of improvement was outweighed by differences associated with income and wealth inequality. CGM can provide population-level insights into the adequacy of glycemic control.

Association of Observed Average Blood Glucose and A1C-Estimated Average Glucose in Hospitalized Patients with Diabetes

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Objective:
A1C is used to gauge the level of outpatient glycemic control when determining an inpatient antihyperglycemic regimen. We evaluated concordance between observed average glucose (OAG) and A1C-estimated average glucose (eAG) in hospitalized patients with diabetes.

Method:
Retrospective analysis was performed using N=937,837 blood glucose measurements from N=17,903 unique adult patients over five years. The ratio of OAG to eAG was used to identify patient phenotypes based on percentile: concordant (within IQR), observed less than expected (<25th percentile), and observed greater than expected (>75th percentile). Multivariable logistic regressions were used to evaluate clinical, patient, and hospital factors associated with either discordant phenotype.

Result:
Factors (adjusted OR; 95% CI) associated with lower OAG than eAG include: female sex (1.09; 1.00-1.18), black race (1.68; 1.54-1.83), higher hemoglobin (1.11; 1.09-1.14), higher total daily insulin dose (1.01; 1.00-1.01), carbohydrate-controlled diet (1.39; 1.27-1.52), NPO/liquid diet (1.18; 1.04-1.34), and taking home insulin (1.27; 1.16-1.39). Factors associated with higher OAG than eAG include: discharge from Intermediate Care Unit (1.21; 1.07-1.37), discharge from a surgical or procedural unit (7.37; 1.18-46.02), higher systolic blood pressure (1.01; 1.00-1.01), tachycardia (1.22; 1.12-1.33), higher respiratory rate (1.04; 1.02-1.06), higher potassium (1.08; 1.02-1.14), higher total daily insulin dose (1.00; 1.00-1.01), and high steroid dose (2.82; 2.50-3.18).

Conclusion:
Inpatient glucose levels are lower than expected based on A1C in women, blacks, patients on carbohydrate-controlled or NPO/liquid diets, and those receiving home insulin or higher inpatient insulin doses. Conversely, inpatient glucose levels are higher than expected in patients admitted to surgical or intermediate care units, those receiving high dose steroids or higher insulin doses, and those with higher potassium levels or vital sign indicators of more severe illness.

One- to Six-Month Forecasts of Time-in-Range

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Objective:
Time-in-range is increasingly of interest as a metric of diabetes management. Accurate predictions of changing time-in-range can support timely delivery of treatment and lifestyle recommendations, leading to improved outcomes. We used continuous glucose monitoring (CGM) data and other health and self-care data collected in the One Drop app to forecast individual's changes in 30-day time-in-range from one to six months in advance.

Method:
Data were used to train a suite of patent-pending supervised machine learning models, each for a different time horizon: 1-2, 2-3, 3-4, or 4-6 months. Data collected prior to 2019 were used for training; data from January 2019 through February 2020 were used for testing. The test set comprised over 67,000 predictions. Prediction root mean square error (RMSE) was compared to the RMSE that would result from assuming persistence (no change from current values). Population subsets were identified, based on information available at prediction time, for whom predictions were more accurate.

Result:
Error reduction relative to persistence varied by forecast horizon and population subset. For 30-day time-in-range, persistence RMSE ranged from 12.1-17.6%, while model RMSE ranged from 7.1-11.8%. Error reductions ranged from 22.2-41.2% relative to persistence.

Conclusion:
Machine learning models based on app-collected CGM, health, and self-care data can predict changes in time-in-range up to six months in advance. These predictions can contribute to prioritizing interventions and guiding self-care, potentially improving outcomes.

Early Insights from a Digitally Enhanced Diabetes Self-Management Education and Support Program

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Objective:
Translation of diabetes self-management education and support (DSMES) into a digital format can improve access, but few digital programs have demonstrated outcomes using rigorous evaluation metrics. This pilot shares early insights into the impact of a digital DSMES program on glycemic control for type 2 diabetes.

Method:
A single-arm, non-randomized trial was conducted to evaluate a digital DSMES program that includes remote monitoring and lifestyle change, in addition to comprehensive diabetes education, staffed by a diabetes specialist. A sample of N=195 participants were virtually recruited using an online research platform. The primary outcome was change in laboratory-tested hemoglobin A1c from baseline to 4 months, and secondary outcomes included change in lipids, diabetes distress, and medication adherence.

Result:
At baseline, participants had a mean A1c of 8.9% (SD=1.9) and mean BMI of 37.5 kg/m^2 (SD=8.3). The average age was 45.1 years (SD=8.9), 70% were women, and 72% were White. At 4-month follow-up, the A1c decreased by 0.8% (p=.001, 95% CI [-1.1, -0.5]) for the total population and decreased by 1.4% (p=.001, 95% CI [-1.8, -0.9]) for those with worse glucose control at baseline (A1c = 9.0%+). Diabetes distress and medication adherence were also significantly improved between baseline and follow-up.

Conclusion:
This study provides early evidence that a digitally enhanced DSMES program improves glycemic control and disease self-management outcomes.

Role of Site Selection & Cannula Length in Insulin Infusion Set Performance

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Objective:
During type 1 diabetes (T1D) pump therapy, an insulin infusion set (IIS) with varied cannula length may be placed in the abdomen, arm, thigh, or buttocks based on personal preference. In this work, the impact of IIS site selection on IIS wear duration and total daily insulin dose (TDD) was assessed in a pre-clinical T1D porcine model and the effect of cannula length with the same characteristics was evaluated in two adult T1D clinical trials.

Method:
In the T1D porcine studies, an IIS with 43" tubing was placed in the dorsum (skin-thickness 3.5-5μm, n=24) or abdomen (skin-thickness 2.8-3.4μm, n=56). Insulin was infused for glycemic control for up-to 7 days. In two adult T1D clinical trials, an IIS with 43" tubing and 6-mm (total n=43) or 9-mm (total n=143) cannula was worn primarily in the abdomen (>90%) with insulin infused for glycemic control for up-to 7 days. The IIS wear duration and mean TDD were determined for both the pre-clinical and clinical studies.

Result:
In the porcine model, there was no significant difference between the IIS survival curves for the dorsum and the abdomen locations. However, TDD was significantly greater in the dorsum (25-30 U/day) compared to the abdomen (15-20 U/day). In both clinical trials, survival curves of the IIS with 6-mm and 9-mm cannula showed no significant difference. However, TDD over 7 days (43.8-48.1 U/day) in the 9-mm group was more stable over time with smaller day-to-day variations, compared to the TDD in the 6-mm group (45.8-54.6 U/day).

Conclusion:
These data indicate that cannula length & site selection may play a significant role in TDD. Additional studies are required to make more definitive conclusions.

Performance of a Factory-Calibrated Continuous Glucose Monitoring (CGM) System with a Retuned Algorithm

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Objective:
The algorithm of a factory-calibrated CGM system (Dexcom G6) was retuned to improve data availability. Its performance was assessed by reprocessing raw data from a large clinical trial.

Method:
Participants ages 6+ years with insulin-treated diabetes were enrolled at 11 U.S. sites to assess Dexcom G6 CGM system performance (NCT02880267). In-clinic visits for frequent comparative blood glucose measurements using YSI were conducted on days 1, 4-5, 7, and/or 10 of system use and varied in length based on participant age. Raw sensor data were reprocessed with the retuned algorithm. Accuracy evaluation included the proportion of CGM values that were within ±20% of YSI reference value for glucose levels ≥70 mg/dL and ±20 mg/dL for YSI glucose levels <70 mg/dL (%20/20) as well as the mean absolute relative difference (MARD) between temporally matched CGM and YSI values. Data availability was calculated by capturing the frequency of intermittently missed readings for sensors that lasted the full sensor wear period.

Result:
Three hundred eighty participants enrolled and N=325 were included in the performance evaluation. There was a 1.4% increase in percentage of sensors with more than 90% of readings with the retuned algorithm compared to the original algorithm. Overall performance was retained: with the new algorithm, %20/20 overall, for adults, and for children ages 6-17 years was 91.8%, 91.8%, and 92.0%, respectively, compared to 91.7%, 91.6%, and 92.0% for the original algorithm. MARD was unchanged and was 9.8%, 9.9%, and 9.6% overall, for adults, and for children, respectively.

Conclusion:
Modifications to the algorithm of a factory-calibrated CGM system improved data availability without substantially affecting system performance. Increased data availability may improve patient experience and may allow CGM data incorporation into automated insulin delivery systems.